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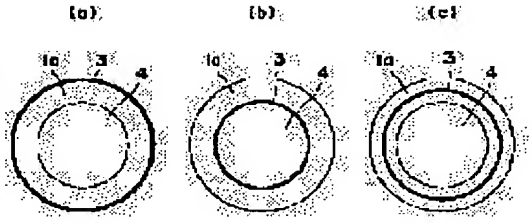
(54) MEDICINE SUPPORTING BODY AND ITS USE

(57)Abstract:
PROBLEM TO BE SOLVED: To obtain a medicine supporting body capable of actualizing the administration of a medicine such as an anticancer agent, etc., in a high concentration in a specific part, by destroying the medicine carrier such as a capsule, etc., supporting the medicine such as the anticancer agent at the specific part such as a blood vessel in a carcinoma tissue or the surface of skin by using an ultrasonic wave surely and by a simple operation and to provide a method for using the medicine supporting body.
SOLUTION: This supporting body for treating medicine contains an ultrasonic sensitive substance 3. A medicine supporting body which contains, is stuck with or covered with the ultrasonic sensitive substance 3 and has a hollow part 4 formed by a shell wall 1a is preferable as the medicine supporting body. In this case, the shell wall 1a contains, is stuck with or covered with the ultrasonic sensitive substance 3 in a laminar state or contains or is stuck with the ultrasonic sensitive substance 3 in a bulky dispersed state.



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* NOTICES *

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CLAIMS

[Claim(s)]
[Claim 1] The drug bearing body containing the ultrasonic susceptibility matter [claim 2] The drug bearing body according to claim 1 which has the centrum formed of **** which made the ultrasonic susceptibility matter contain, adhere or cover [claim 3] The drug bearing body according to claim 2 with which said ultrasonic susceptibility matter is contained, adhered or covered with the layer condition by said ****.
[Claim 4] The drug bearing body according to claim 2 with which said **** contains or adheres to said ultrasonic susceptibility matter in the condition of having distributed massive.
[Claim 5] The drug bearing body according to claim 2 to 4 whose thickness of said **** is 0.001-50 micrometers.
[Claim 6] The drug bearing body according to claim 2 to 5 characterized by making a drug **** to the centrum formed of said ****.
[Claim 7] The drug bearing body according to claim 6 characterized by making said centrum **** said drug in the condition of having made it ****ing with gas [claim 8] The drug bearing body according to claim 1 to 7 with which said ultrasonic susceptibility matter is characterized by being a porphyrin derivative or a xanthene derivative [claim 9] Operation of said drug bearing body characterized by destroying said drug support by irradiating the supersonic wave of an output sentimental [square] 0.1-1000W /at a drug bearing body according to claim 1 to 8.

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DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] About the technique of performing various kinds of therapies using supersonic vibration, especially, this invention controls administration of a drug and relates to the therapy promoting agent for emitting a drug effectively in a specific part in the living body using supersonic vibration.
[0002]
[Description of the Prior Art] Current cancer treatment is divided roughly into the two approaches of extinction of the cancer cell by extraction of the cancer organization by operation, or the anticancer drug object. Extraction of the cancer organization by operation can be performed, only when it is limited to the part where cancer is narrow or transition is not accepted, but on the other hand, the chemotherapy of cancer has a dramatically strong side effect, and the nausea by the medication of a large quantity, much renal dysfunction, and many impaired liver functions are accepted. And cancer reacts only to a high-concentration drug and the chemotherapy of cancer is not obtaining not much high **** results.
[0003] Many attempts are made to current and these problems. Although the approach called the missile therapy of an anticancer agent is an approach of applying the antibody combined selectively to a cancer cell as an anticancer agent, and making an anticancer agent acting on a cancer cell intensively, effectiveness sufficient for the moment is not acquired.
[0004] On the other hand, the inside of the body is injected with containment and it at drug bearing bodies, such as a capsule which consists an anticancer agent of specific matter, the method of prescribing the high-concentration anticancer agent by ** Li and the limited part for the patient for the husks is devised within the blood vessel near the cancer, and the effectiveness is proved in the experiment etc.
[0005] However, the method of tearing capsule husks efficiently in the above-mentioned approach is not yet established. Although various research of embedding a thermo sensor, a hydrogen ion exponent sensor, etc. which applied the polymer etc. to capsule husks, and inducing bleedoff of a drug on a certain temperature or hydrogen ion exponent conditions until now is done, it is dramatically difficult to set temperature and the conditions of a hydrogen ion exponent as arbitration near the tumor site.
[0006] Moreover, the approach to which destroy capsule husks with the impulse wave and ultrasonic energy from the outside, and an internal drug is made to emit was also considered.
[0007] For example, the approach of destroying the liposome which contains gas and a drug in a U.S. Pat. No. 5580575 description with a supersonic wave by the predetermined part of the patient inside of the body is indicated.
[0008] However, since powerful ultrasonic irradiation will be needed and the resonant frequency will be determined by the amount of the gas in a capsule in order to destroy capsules, such as liposome, mechanically only by oscillation of a supersonic wave in this way, it is difficult to destroy a capsule except the ultrasonic frequency.
[0009] Thus, in the activity of acoustical energy, although remarkable accuracy was required of the exposure setting out, in the tumor site, it was not easy to realize an exact ultrasonic

frequency and reinforcement.
[0010]
[Problem(s) to be Solved by the Invention] This invention makes it the technical problem to offer the drug support which makes it possible to realize high-concentration administration in said specific part of drugs, such as said anticancer agent, and its operation by destroying certainly drug bearing bodies, such as a capsule which ****(ed) drugs, such as an anticancer agent, by simple actuation using a supersonic wave in a specific part like the blood vessel of a cancer in-house, or a skin front face.
[0011]
[Means for Solving the Problem] In order to solve the above-mentioned technical problem, in invention concerning claim 1 of this application, it carried out to making a drug bearing body contain the ultrasonic susceptibility matter.
[0012] In invention concerning claim 2, what has the centrum formed as said drug bearing body of **** which made the ultrasonic susceptibility matter contain, adhere or cover was adopted.
[0013] Said **** was made to contain, adhere or cover said ultrasonic susceptibility matter with a layer condition by invention concerning claim 3.
[0014] Said ultrasonic susceptibility matter was made to contain or adhere to said **** in the condition of having distributed massive, by invention concerning claim 4.
[0015] Invention concerning claim 5 prescribed the thickness of said **** to the range of 0.001-50 micrometers.
[0016] The drug was made to **** to the centrum formed of said **** in invention concerning claim 6.
[0017] Said centrum was made to **** said drug in the condition of having made it ****ing with gas, by invention concerning claim 7.
[0018] In invention concerning claim 8, the porphyrin derivative or the xanthene derivative was adopted as ultrasonic susceptibility matter.
[0019] In invention concerning claim 9, we decided to destroy said drug support by irradiating the supersonic wave of an output sentimental [square] 0.1-1000W /at a drug bearing body.
[0020]
[Embodiment of the Invention] This invention has the 1st description to make said ultrasonic susceptibility matter produce a chemical change or a physical change, destroy said drug bearing body, and make a drug emit, when said drug bearing body which ****(ed) the drug by including the ultrasonic susceptibility matter in the drug bearing body which the drug for a therapy is **** (ed) and can be conveyed to the object part is able to irradiate a supersonic wave in the object part.
[0021] Since destruction of this capsule is not influenced so much by the exposure conditions of a supersonic wave as compared with the approach to which destroy capsule husks only in the oscillating operation by the supersonic wave, and an internal drug is made to emit, this invention can adopt the ultrasonic energy of the comparatively large range that it is [square] sentimental 0.1-1000W /.
[0022] Therefore, like before, without performing conditioning of very difficult ultrasonic irradiation, in the object part in the living body, this drug bearing body can be destroyed effectively and a drug can be emitted also by supersonic waves other than the resonant frequency of a drug bearing body.
[0023] Moreover, this invention has the 2nd description to form a centrum and make this **** contain, adhere or cover the ultrasonic susceptibility matter with **** which has predetermined thickness in a drug bearing body. That is, while drug support can bear mechanical energies, such as a pressure, enough, it is designed by the structure which breaks easily according to the chemical change or physical change of said ultrasonic susceptibility matter.
[0024] The configuration of drug support is made into the shape of a capsule etc., it is massive, and, specifically, the ultrasonic susceptibility matter is contained, adhered or covered by a layer condition or **** which constitutes a capsule. It becomes possible, when said ultrasonic susceptibility matter is in the layer condition to have the effect of deterioration of this ultrasonic susceptibility matter on said whole ****, and on the other hand, when said ultrasonic

susceptibility matter is massive, it becomes possible by making this ultrasonic susceptibility matter exist in said **** locally to destroy this **** certainly. In addition, what was mixed to homogeneity may be used for the substrate ingredient which mentions the ultrasonic susceptibility matter later as an own component of drug support. In this case, while destruction of **** is performed uniformly, manufacture of drug support becomes easy.

[0025] Furthermore, although this invention is made to **** a drug to the centrum formed of said ****, it has the 3rd description for the gas of the specified quantity to be made to exist in said centrum with said drug. Although the class and amount of said gas are arbitrary so that it may mention later, it is desirable to be set up in 0.01 - 50% of range of the volume of said centrum. First, the component and structure of a drug bearing body concerning this invention are explained.

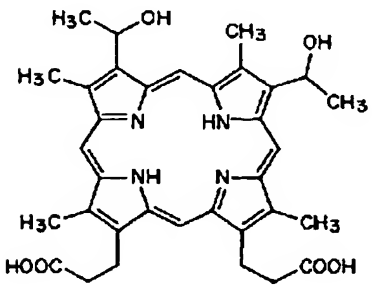
[0026] Although a "drug bearing body" is the carrier which the drug for a therapy is ****(ed) and can be conveyed to the inside of the body or the object part of a body surface here and especially the configuration is not limited, the capsule configuration which has the centrum carried out by **** the external world and ** exception is desirable, in view of the ease of manufacture, a manufacturing cost, etc.

[0027] The magnitude of a drug bearing body is usually suitably set up in 0.01-100 micrometers. In less than 0.01 micrometers, it is excreted by the outside of the body and effectiveness becomes imperfection, and when larger than 100 micrometers, the danger of causing a blood-flow failure is in a blood vessel.

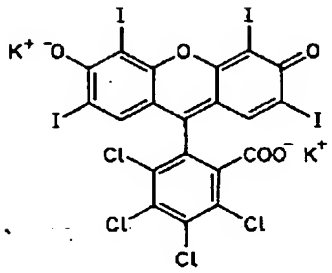
[0028] As a substrate ingredient which constitutes said drug bearing body, matter, such as various kinds of living body adaptation polymers, albumin, liposome, and sugar, can be used.

[0029] Moreover, improvement of the alternative translatability of an about [target group Oribe], water-soluble increment, acceleration of absorption, or relief of a side effect can also be aimed at by using the drug bearing body to which prodrug-ized qualification was performed. In this case, after attaining the object of said qualification in the inside of the body, it is restored to the original drug bearing body enzyme-wise or nonenzymatic, and it becomes possible to recover the susceptibility over a supersonic wave etc. The drug bearing body to which prodrug-ized qualification was performed is contained under the category of this invention. In addition, what performed prodrug-ized processing may be suitably used for the drug ****(ed) by the drug bearing body.

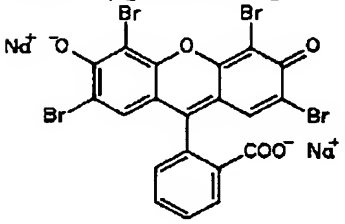
[0030] The "ultrasonic susceptibility matter" is matter which produces a certain change of changing structure of self [**** / producing a chemical change] to the matter of self [**** / activating through various devices], or others with the supersonic wave equipped with a predetermined frequency and reinforcement so that it may mention later. As said ultrasonic susceptibility matter, although a FURORE scene (fluorescein), merocyanine, etc. are mentioned, a porphyrin derivative or a xanthene derivative is desirable in respect of the compatibility to a toxic field and a toxic living body. It is the hematoporphyrin and [Formula 1] which specifically have the structure expression shown below as said porphyrin derivative or a xanthene derivative.



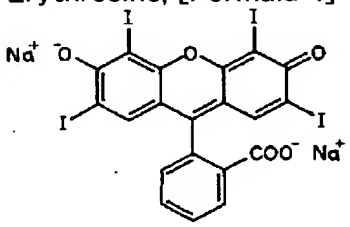
A rose bengal, [Formula 2]



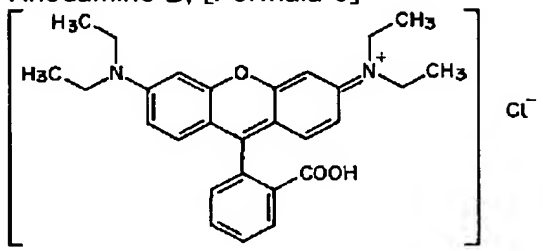
Eosin Y, [Formula 3]



Erythrosine, [Formula 4]



Rhodamine B, [Formula 5]



**********.

[0031] And although the lump of a drug 2 and the ultrasonic susceptibility matter 3 be distribute at suitable spacing in the drug bearing body 1 of an infinite form as structure of a drug bearing body so that it may be indicate by drawing 1 , it be desirable to form a centrum and to make this **** contain , adhere or cover the above-mentioned ultrasonic susceptibility matter with **** which have predetermined thickness in the drug bearing body itself at the point which enable effective destruction of this drug support .

[0032] As long as said centrum is formed in the interior of a drug bearing body, especially the number may not be limited, may be one, or may be plural. Moreover, although especially the formation part is not limited, either, in order to emit a drug good, it is desirable to be formed in the surface section of a drug bearing body. In addition, making the configuration of a drug bearing body itself into the shape of a capsule constituted by the layer of **** which has said predetermined thickness is also included in the range of this invention.

[0033] Here, the thickness of said **** is usually determined within the limits of 0.001-50 micrometers. When the thickness of **** is set to less than 0.001 micrometers, **** becomes destroyed [tend] by the impact, and before arriving at the object part in the living body, a possibility that said **** may be destroyed and an internal drug may flow out is. On the other hand, if set to 50 micrometers or more, even if it will become difficult to destroy said **** also according to an operation of the ultrasonic susceptibility matter and a part of **** will be

destroyed, the amount of husks wall which cannot be destroyed will remain, and there will be a possibility of barring bleedoff of a drug.

[0034] When it makes it face to contain the ultrasonic susceptibility matter to a drug bearing body and this drug bearing body is equipped with husks box-frame construction, it is desirable to make said ultrasonic susceptibility matter contain, adhere or cover in this ****.

[0035] The layer of the ultrasonic susceptibility matter 3 may specifically be covered to the outside surface of **** 1a, as shown in drawing 2 R> 2 (a), or the inner skin of **** 1a may be coated like drawing 2 (b), and you may make it exist in the interior of **** 1a in the state of a layer like drawing 2 (c). In addition, the layer of the ultrasonic susceptibility matter 3 does not need to be a continuous layer system as shown in drawing 2 , and it is not necessary to make it exist in **** 1a and concentric circular.

[0036] Moreover, the ultrasonic susceptibility matter 3 may be made to contain or adhere to **** 1a in the condition of having made it distributing massive. That is, as shown in drawing 3 (a) and drawing 3 (b), the lump of the ultrasonic susceptibility matter 3 may be made to adhere to the outside surface and internal surface of said **** 1a, and you may distribute suitably for the interior of said **** 1a like drawing 3 (c). In this case, each lump may project in part from ****1a, and does not need to project.

[0037] And as shown in drawing 3 (d), it is good also as structure which the lump of the ultrasonic susceptibility matter 3 penetrates **** 1a, and the part exposes to the external world and a building envelope, respectively. If it is when shown in drawing 3 , you may be distributing to homogeneity at said **** 1a, and the lump of said ultrasonic susceptibility matter 3 may be distributed for roughness and fineness. Moreover, especially each lump's configuration may not be limited and may be various configurations other than a globular form.

[0038] In addition, in drawing 2 and drawing 3 , 4 is the centrum formed of **** 1a, and the drug of a predetermined class is ****(ed) by this centrum.

[0039] Next, it explains, referring to drawing 4 about the operation of the drug bearing body mentioned above.

[0040] The above-mentioned drug bearing body which ****(ed) the drug of a predetermined class is injected into the inside of the body by the ion TOFORESHISU technique using the drug bearing body which used medication implements, such as a syringe, or was ionized by internal use, dermal administration, or the special approach etc.

[0041] And when the activity of a catheter or an endoscope is possible, the ultrasonic generating component for a therapy is introduced into the inside of the body of installation and a patient at the head of a catheter or an endoscope, and is made to reach the affected part.

[0042] Drawing 4 (a) and drawing 4 (b) are the sectional views showing the installation mode of the ultrasonic generating component used in operation of this invention, respectively, and drawing 4 (a) shows structure when drawing 4 (b) attaches the structure at the time of attaching an ultrasonic generating component in the point of an endoscope in the point of a catheter again.

[0043] In the mode shown in drawing 4 (a), the very small central canal 6 including wiring for operating the optical fiber and the supersonic vibration component mentioned later which is not illustrated is installed in the interior of the capillary 5 which constitutes an endoscope, and the 1st cylindrical shape-like supersonic vibration component 9 and the 2nd supersonic vibration component 10 which have a centrum in the direction of an axis at the head of a capillary 5 are arranged in concentric circular. As a supersonic vibration component, what attached the electrode in both sides of a piezoelectric device, for example is mentioned, and a supersonic wave is emitted by impressing the electrical signal of an ultrasonic frequency to this inter-electrode one in this case. 8 is the core section for transmitting to the optical fiber which does not illustrate an external image, and is embedded at said centrum. Moreover, the gap of a capillary 5 and the very small central canal 6 is made into the drug supply way 7, and is connected with the breakthrough 11 which carries out opening at suitable spacing for the peripheral surface by the side of the head of a capillary 5.

[0044] And each frequency characteristics differ, by controlling both actuation, two kinds of frequencies are mixed and said 1st supersonic vibration component 9 and the 2nd supersonic

vibration component 10 are oscillated in the direction (the direction of an arrow head) where the shaft orientations of an endoscope are vertical. Thus, it emanates combining two or more kinds of supersonic waves because the destructive effectiveness of direction of a complicated supersonic-wave wave of a drug bearing body improves. In addition, the 1st [which has the above-mentioned structure], and 2nd supersonic vibration components may be attached at the head of a catheter. On the other hand, the laminating is carried out in the direction of an axis of a catheter, both the 1st ultrasonic oscillation component 9 and 2nd ultrasonic oscillation component 10 from which frequency characteristics differ in the mode shown in drawing 4 R> 4 (b) being used as the shape of a cylindrical shape of a solid.

[0045] Therefore, the supersonic wave which has two kinds of frequencies in the direction of an axis of a catheter (the direction of an arrow head) is oscillated by controlling both actuation.

[0046] In addition, the 1st [which has the above-mentioned structure], and 2nd supersonic vibration components may be attached at the head of an endoscope.

[0047] Now, a drug bearing body is turned and emitted to the affected part from the drug supply way 7 through opening 11 after checking that the head of an endoscope or a catheter has arrived at the affected part organization. it -- simultaneously -- or after predetermined time progress -- super- -- if the 1st and 2nd supersonic vibration components are operated, the supersonic wave with which frequencies differ will be emitted to the affected part, and will destroy the drug bearing body which exists during an affected part organization. Therefore, the drug in a drug bearing body is limited and prescribed for the patient only around an affected part organization part.

[0048] It is desirable to choose a device in consideration of the relative position of the affected part to said endoscope or catheter, so that the exposure of a suitable supersonic wave may be obtained. Moreover, the diameter of said endoscope or a catheter can use the thing of the range of about 5cm from 1mm, choosing it suitably.

[0049] In addition, three or more sorts of above-mentioned ultrasonic oscillation components may be attached. In that case, since a still more complicated ultrasonic wave is generable, the destructive effectiveness of a drug bearing body improves further. When it is the configuration which a drug bearing body is easy to be destroyed, the supersonic vibration component of 1 may be used.

[0050] two or more sonicators for a therapy which carried out the laminating of the 1st supersonic vibration component 9 which have the property same with having describe above to the crevice of the base 12 which consist of flexible synthetic resin etc. as show in drawing 5 , and the 2nd supersonic vibration component 10 , and have arrange them on the other hand when neither a catheter nor an endoscope can be use be preferably lay on the skin corresponding to the affected part , and a supersonic wave be turn to the affected part (the direction of an arrow head) , and be irradiate . It is desirable to prepare two or more laminated material of a supersonic vibration component in a base 12 so that it may illustrate. Since a base 12 can curve according to the configuration of a patient's body, it can centralize a supersonic wave on the affected part. The diameter of said 1st and 2nd supersonic vibration components is usually suitably set up in 5cm - 10cm. In addition, said 1st supersonic vibration component 9 and the 2nd supersonic vibration component 10 have it, in order that the direction which consists of oscillation ingredients with flexibility like a fluorine compound may maintain the flexibility of the whole equipment and may secure the adhesion to the skin etc. [desirable]

[0051] And the ultrasonic energy concentrated on the affected part destroys the drug bearing body which exists there, and emits an internal drug to the affected part.

[0052] Thus, in this invention, destruction becomes possible [destroying the difficult drug bearing body easily, setting at least inside the desired body, and controlling bleedoff of a drug] only ultrasonically by including the ultrasonic susceptibility matter in a drug bearing body.

[0053] In addition, since a drug bearing body can be made to accumulate on an affected part organization when matter, such as an antibody selectively combined with affected part organizations, such as a cancer cell, a thrombus, an organ, and a blood vessel that carried out arteriosclerosis, is included in the substrate ingredient of a drug bearing body, it becomes possible to destroy the drug bearing body accumulated on this affected part organization using a

supersonic wave, and to medicate high concentration with a drug locally.
[0054] Next, the conditions of the supersonic wave used in this invention are explained.
[0055] The output of the supersonic wave irradiated for destruction of the drug bearing body concerning this invention is suitably set up in the range sentimental [square] 0.1-1000W /. If the outputs of a supersonic wave are two or less 0.1 W/cm, only the energy which activates the ultrasonic susceptibility matter runs short, and since there is too much heat release when it becomes two or more 1000 W/cm, a damage will be given to a living body.
[0056] Moreover, although the frequency of a supersonic wave is suitably set up in 10kHz - 100MHz, the range of 20kHz - 10MHz is desirable especially. According to the supersonic wave of this frequency band, it becomes possible to generate the cavitation later mentioned with comparatively low energy, and to destroy a drug bearing body efficiently.
[0057] And as mentioned above, it is also possible to activate the ultrasonic susceptibility matter more efficiently by combining two or more frequencies, and to destroy a drug bearing body. For example, while irradiating the supersonic wave of a fixed frequency, intermittently, this is changing to a different frequency, generating of the cavitation mentioned later can be reinforced intentionally, or it controls, and a drug bearing body can be destroyed or disassembled.
[0058] When the example was given, while carrying out continuous irradiation of the supersonic wave to the affected part by 100kHz, much more destructive effectiveness was acquired by changing to the frequency of 270kHz in the shape of a short-time (0.001sec-10sec) pulse. The same effectiveness is expected, even if it is fixed within the limits and carries out continuation adjustable [of the frequency of a supersonic wave]. This phenomenon is considered that destructive power increased by stopping resonance motion of a drug bearing body temporarily.
[0059] Here, the device of destruction of a drug bearing body is explained.
[0060] If the ultrasonic energy beyond the value which is among a liquid is generally given, the minute air ball called cavitation will occur. It is related with the generating mechanism of cavitation. For example Robert E.Apfel:"Sonic effervescence:tutorial on acoustic cavitation", Journal of Acoustic Society of America 101(3):1227-1237 and March 1997, Atchley A, and Crum L:"Ultrasound-Its chemical, Physical and biological effects:Acoustic cavitation and bubble dynamics", and Ed Although indicated by Suslick K, pp 1-64, 1988 VCH Publishers, and New York, it explains briefly [below]. Cavitation is that the gas which has melted into the water solution serves as air bubbles, or the very very small bubble which had already existed repeats an oscillation or amplification, and a cutback, and turns into air bubbles under a certain acoustical oscillation.
[0061] And if this cavitation becomes the magnitude of extent which cannot maintain that magnitude, it will collapse, but since this breaking takes place rapidly, it is known that various energy will occur locally then.
[0062] That is, in the case of breaking of the above-mentioned cavitation, the hot spot of 6000 - 7000 degrees is formed in the core, and various energy other than mechanical energies, such as an oscillation, such as electromagnetic waves, such as a visible ray and ultraviolet rays, heat, plasma, electromagnetic field, a shock wave, a free radical, and heat, is considered to generate locally.
[0063] It is thought that it activates with the above-mentioned various energy produced in the case of cavitation breaking, or the ultrasonic susceptibility matter in this invention produces a chemical change, or changes structure.
[0064] For example, the rose bengal which is one of the ultrasonic susceptibility matter in this invention is excited and activated by light or ultraviolet rays with a wavelength of 530nm. Therefore, it is thought that activation of a rose bengal is caused by the ultraviolet rays generated in the case of cavitation breaking.
[0065] By the way, in the liquid with which the ultrasonic susceptibility matter exists, it is known that the threshold of the ultrasonic energy for cavitation generating will become low. Therefore, the ultrasonic susceptibility matter contained in the drug bearing body does so the effectiveness of activation etc. acting as itself and destroying a drug bearing body with the energy which carried out induction of the cavitation generating near the drug bearing body selectively, and was produced by breaking of cavitation.

[0066] Also when the minute bubble exists in a liquid on the other hand, it is known that the threshold of the ultrasonic energy for cavitation generating will become low.
[0067] Therefore, by making the gas of the specified quantity exist in drug support, cavitation is effectively generated at the time of ultrasonic irradiation, and the energy produced in the case of this cavitation breaking can be used effective in destruction of drug support. Although the class and amount of said gas are arbitrary, as for the amount, it is desirable to be set up in 0.01 - 50% of range of the volume of the centrum in a drug bearing body. If the cause of the generating of cavitation cannot be effectively carried out to the amount of said gas being said less than 0.01% of centrum volume and the amount of said gas exceeds said 50% of centrum volume, the reinforcement of a drug bearing body will not be maintained and the amount of the medicine conveyed will be restricted until it arrives at the object part.
[0068] In addition, it is also possible to use for the therapy of an affected part organization directly using various energy, such as electromagnetic waves, such as a visible ray produced in the case of breaking of cavitation and ultraviolet rays, heat, plasma, electromagnetic field, a shock wave, a free radical, and heat.
[0069] For example, by generating a supersonic wave near the affected part organization, the ultraviolet rays which are usually absorbed by the skin and do not reach the inside of the body are generated near the affected part tissue in the living body by breaking of the cavitation originating in a supersonic wave, and it becomes possible to treat the affected part by the germicidal action.
[0070] That is, cavitation is generated with a supersonic wave in a body, and the approach of treating the affected part with the energy produced at the time of this breaking can be enforced.

[0071] Since according to this approach energy, such as ultraviolet rays, is generated free in all parts in the living body and the affected part is treated by this, it is not necessary to take into consideration the effect by the side effect of a proper to medication.
[0072] This invention can be carried out with a gestalt which is described below.
[0073] [Cancer treatment] The intravenous injection of what coated the outside surface of this capsule with a package and the ultrasonic susceptibility matter for the cisplatin which is an anticancer agent by the capsule of a polymer is given. Since cisplatin is covered by the polymer, even if the intravenous injection of said capsule is given, it does not have toxicity (side effect), and is only flowing the inside of blood.
[0074] However, if a supersonic wave is irradiated while said capsule is flowing the inside of the blood vessel under cancer organization, the ultrasonic susceptibility matter on said front face of a capsule will be activated, the capsule which has wrapped cisplatin will be disassembled, and cisplatin will be emitted by high concentration all over this organization.
[0075] Therefore, while administration of the high-concentration anticancer agent in the limited part in which cancer is located is attained, a normal cellular structure becomes possible [escaping the strong toxicity of cisplatin].
[0076] As for this approach, effectiveness is acquired by especially diseases in which many blood vessels exist, such as liver cancer and a brain tumor. As the exposure approach of a supersonic wave, a neoplasm part can be irradiated from the front face of the skin, or a direct supersonic wave can also be irradiated in a cancer organization during a laparotomy.
[0077] Moreover, it is also possible to an endoscope to irradiate a supersonic wave for an ultrasonic component from the interior of installation and the body, and a direct supersonic wave can also be irradiated from the inside cavity of the interior of stomach, or the large intestine in that case at colon cancer etc.
[0078] According to a case, a suitable path is chosen from various roots, such as impregnation, dermal administration, etc. to the direct affected part, via the absorption from the intestinal tract according [the route of administration of the above-mentioned capsule] to internal use besides an intravenous injection, and a lymphatic duct.
[0079] By the way, since Foto Phi Lynne herself has the compatibility over a cancer cell when Foto Phi Lynne is used as the above-mentioned ultrasonic susceptibility matter, it concentrates on a cancer organization and the above-mentioned capsule containing cisplatin is accumulated in

high concentration.
[0080] And it becomes possible by irradiating a supersonic wave in this condition to prescribe cisplatin for the patient further during a cancer organization at high concentration.
[0081] In addition, since Foto Phi Lynne also has the property which produces a killer cell operation when it activates with a supersonic wave, in this case, it combines with cisplatin and an anticancer operation is reinforced in multiplication.
[0082] Moreover, in the case of the cancer and vesical cancer which were transferred to intraperitoneal, direct intraperitoneal is injected with the capsule which connotes an anticancer agent, and how to turn a supersonic wave to the whole abdominal cavity, and irradiate it from a skin front face, can be considered after that. The case of vesical cancer can make said capsule full [in a bladder] from an urethra, and vesical cancer can be treated by irradiating a supersonic wave from the skin front face of the hypogastrium. While irradiating the supersonic wave for a therapy in these cases, it has the advantage that the bleedoff condition of a drug is observable with the supersonic wave for a diagnosis.
[0083] [Thrombolytic treatment] The thrombolytic agent is used as a remedy of myocardial infarction or cerebral infarction. However, in order to dissolve a thrombus as early as possible, when a medicine is prescribed for the patient so much, there is risk of being hard coming to solidify blood conversely and causing many bleeding.
[0084] Then, it injects with a package and this in a blood vessel by the capsule of the living body adaptation polymer which contains the ultrasonic susceptibility matter for thrombolytic agents, such as urokinase, or the product made from albumin. In the usual condition, since it is not destroyed, this capsule does not cause a solvent action within a blood vessel.
[0085] And if said capsule arrives at the part to which thrombuses, such as a peripheral vessel of a coronary artery, exist, for example in the case of myocardial infarction, by irradiating a supersonic wave from the outside of the body or the inside of the body using equipment which was described above, said capsule will be destroyed and a thrombolytic agent will be locally emitted by high concentration.
[0086] specifically, it is shown in drawing 6 -- as -- up to near the thrombus -- the catheter with an ultrasonic radiator or endoscope of drawing 4 -- the inside of a blood vessel -- inserting -- the capsule containing a thrombolytic agent -- a thrombus -- it emits from the upstream immediately and a supersonic wave is oscillated simultaneously. Said capsule is destroyed by operation of the ultrasonic susceptibility matter activated by the supersonic wave, and an internal thrombolytic agent is emitted to a thrombus part.
[0087] In addition, in case the capsule which was not destroyed ultrasonically flows and arrives at the affected part again, it is destroyed and used. And since said capsule is not destroyed until it reaches the affected part again, it does not become the factor of bleeding.
[0088] Moreover, when the matter or antibody which is specifically affinitive at a thrombus is beforehand given to the outside surface of a capsule, this capsule piles up a thrombus at high concentration. If a supersonic wave is irradiated to a thrombus part in the condition, it will become possible to destroy this capsule and to prescribe a thrombolytic agent for the patient effectively near the thrombus. It is reported that the matter which has compatibility in a thrombus is Lanza **** (Circulation, 1995, 92.Suppl I:1-260).
[0089] By doing in this way, thrombolytic treatment becomes possible efficiently, without causing side effects, such as bleeding.
[0090] [Blood vessel therapy] When arteriosclerosis etc. becomes a cause and the vasoconstriction happens, the operation therapy which a blood vessel lumen is extended [therapy] with a balloon catheter in recent years, and makes the flow of blood resume is performed briskly.
[0091] Moreover, after the above-mentioned operation, again, a therapy which is fixed where a blood vessel lumen is extended by the metal stent is also briskly performed so that the vasoconstriction may not occur.
[0092] However, a certain amount of breakage is done to the wall of a blood vessel in any case. That a carrier beam blood vessel organization should recover a blood vessel for breakage in the original condition, although restoration accompanied by growth of a blood vessel organization is

performed, the case where too much restoration takes place in this restoration process, and the restenosis of a blood vessel is started goes up to 50% or more, and it considers as the fault of this therapy.

[0093] Then, the thing in which the drug bearing body which ****(ed) Foto Phi Lynne inside was made to mix as construction material of balun is adopted, the balloon catheter which located the ultrasonic generating component in the core is inserted into a blood vessel, balun is expanded in the object part, and it is made to stick to a blood vessel wall, as shown in drawing 7 .

[0094] ** by which the drug bearing body located in the part which touches the blood vessel wall of said balun if a supersonic wave is perpendicularly generated with the axis of said catheter in this condition is destroyed, and internal Foto Phi Lynne is directly poured in into a blood vessel wall.

[0095] Since FOTOFI Lynne has the property which checks the restoration process of a blood vessel organization to some extent when it activates ultrasonically, by balun, she becomes possible [controlling too much restoration of a carrier beam blood vessel wall] about breakage, and can prevent the restenosis.

[0096] In the gestalt of this operation, Foto Phi Lynne is ****(ed) in the drug bearing body as a drug for an affected part therapy, and although the ultrasonic susceptibility matter for this bearing body destruction contained in a drug bearing body is made into arbitration, Foto Phi Lynne may be used as this ultrasonic susceptibility matter.

[0097] In addition, as a drug for an affected part therapy which can be used under a blood vessel therapy, the gene with which a blood vessel wall is medicated, heparin, the radioactive substance, etc. are mentioned.

[0098] [Activity as a hemostat] To hepatic carcinoma, ethanol is poured in into the nutrition blood vessel of current and a cancer organization, breakage is done to the wall of this blood vessel, a thrombus is made artificially, and this blood vessel is closed, or the liquid of a specific class is poured in, and the cure which prevents growth of a cancer cell by blocking a blood vessel etc. is performed.

[0099] Instead, by activating with a supersonic wave, the drug bearing body containing a rose bengal which demonstrates the operation as a blood vessel wall breakage agent, and this pour in simultaneously independently the drug bearing body containing a thrombin which has the operation as coagulant into a blood vessel, and adopt the approach of irradiating a supersonic wave in the affected part.

[0100] With the gestalt of this operation, the rose bengal is ****(ed) in the drug bearing body as a drug for an affected part therapy. And a rose bengal may be used although the ultrasonic susceptibility matter for this bearing body destruction contained in both the drug bearing body is arbitrary.

[0101] In this approach, although said drug bearing body is destroyed by the supersonic wave and the rose bengal of that interior is emitted in the affected part, in that case, the rose bengal itself is activated by the supersonic wave, breakage is done to a blood vessel wall, and a thrombus is formed.

[0102] And the thrombin which could come, simultaneously was emitted from the separate drug bearing body makes blood solidify. Therefore, the blood flow in the affected part is stopped.

[0103] Thus, the synergistic effect as a hemostat can be acquired by combining two sorts of drug bearing bodies.

[0104] Besides the therapy of hepatic carcinoma, the above-mentioned approach is suitable for the hemostasis of the organ bleeding by the traffic accident with which he was hardly able to deal until now.

[0105] [Percutaneous absorption of a drug] About the dermal administration of the drug which used the supersonic wave together, it is just already going to be known. For example, it has many detailed bores and the processor which consists of a disc-like board with which the liquid was contained inside is developed so that it may be indicated by the description of Japanese Patent Application No. No. 166334 [nine to]. In this equipment, it is possible efficiently by making a detailed hole on the surface of the skin using a cavitation generating phenomenon to perform administration of a drug or extraction of body fluid, without being accompanied by the pain.

[0106] With the gestalt of this operation, the drug bearing body which contained the ultrasonic susceptibility matter in said bore in the above-mentioned processor is arranged.
[0107] Hereafter, it explains with reference to drawing 8 .
[0108] In this example, the dermal administration equipment 13 of a drug is constituted from a film which consists of a comparatively thin synthetic-resin ingredient of the range of 1 micrometer - 1cm etc., and the circular space 14 is formed in the interior.
[0109] Two or more bores 16 which are outside open for free passage from the circular space 14 are formed in the bottom side film 15 of dermal administration equipment 13. The diameter of a bore 16 can be made into the range of 0.1mum-3mm. In addition, although the bore 16 is distributed over homogeneity in the example of drawing 8 , in it, it may be prepared in roughness and fineness if needed. Moreover, unfairness, such as not only a circle but stellate, a polygon, etc., is sufficient as the cross-section configuration of a bore 16. The consistency of a bore 16 can be made into 1 per 1 square centimeters to 1 million range.
[0110] On the other hand, the supersonic vibration component 18 is attached in the upside film 17 of dermal administration equipment 13. Although this supersonic vibration component 18 may be formed in one with dermal administration equipment 13, you may make it force this on the upside film 17 of dermal administration equipment 13 as a member which became independent independently.
[0111] It faces using the dermal administration equipment 13 of a drug, the drug bearing body 19 is arranged in a bore 16, and the circular space 14 and the **** space 20 of the drug bearing body 19 interior are filled with the liquid drug 21.
[0112] And the bottom side film 15 of dermal administration equipment 13 is stuck by pressure on the surface of the skin, a driving signal is supplied to the supersonic vibration component 18, and a supersonic wave is generated. Then, while the drug bearing body 19 is destroyed and a bore 16 is opened for traffic, cavitation occurs in the liquid drug 21 in the circular space 14, the liquid flow of the high speed produced at the time of breaking of this cavitation passes a bore 16, the skin is reached, and a detailed hole is formed in that front face. The liquid drug 21 is absorbed by the inside of the body through this hole.
[0113] By doing in this way, even when a bore 16 is comparatively large, a liquid drug does not flow out of a bore 16 at the time of storage of dermal administration equipment 13. On the other hand, since the drug bearing body 19 is destroyed by the supersonic wave, a bore 16 can be made certainly opened for traffic in the case of an activity.
[0114] Moreover, since the ultrasonic susceptibility matter in the drug bearing body 19 reduces the threshold of cavitation generating, cavitation can be generated in the liquid drug 21 with low ultrasonic energy. It becomes possible to lessen by this ultrasonic energy irradiated by the skin, and a possibility of having an adverse effect on the skin decreases.
[0115] As drugs prescribed for the patient into the skin using this equipment, there is an antiallergic agent, an insulin, various hormone, an anticancer agent, an anti-inflammatory agent, an anesthetic, an anticoagulant (heparin, urokinase), an antibiotic, various vitamins, a steroid, a pressure-up agent, a hypotensor, a psychotropic, hair growing, or a depilatory.
[0116] [Infectious disease therapy] Although the sterilization disinfection effectiveness by UV light is known well, UV light is [only being used for disinfection of front faces, such as a medical device, and] in atmospheric air chiefly, in order that the permeability in the inside of a liquid may be very bad and may decline promptly.
[0117] By the way, it is known that sirloin BENGARU which is the ultrasonic susceptibility matter also has the operation which reduces the threshold of cavitation generating by the supersonic wave.
[0118] Then, this property can be used and a supersonic wave can be used for the therapy of the infectious disease outside the inside of the body at the therapy of the infectious disease in the inside of the body.
[0119] Namely, in the infectious disease therapy in the inside of the body, if the bearing body containing a rose bengal is made to invade to the depths of the affected part by injection etc. and a supersonic wave is irradiated towards the affected part in the condition, as cavitation occurred and mentioned already with comparatively low ultrasonic energy on these outskirts of a

bearing body, UV light will occur at the time of the breaking.
[0120] Therefore, UV light is irradiated from point-blank range at the affected part in the living body, and since it becomes possible to sterilize, it becomes possible to apply to the therapy of an infectious disease.
[0121] Moreover, since various antibiotics do not need to be used for this approach, it has the advantage of not making resistant bacteria.
[0122] Next, in the case of a skin infectious disease, it is the drug bearing body which ****(ed) the cutaneous-absorption accelerator, and it applies to a skin front face what covered the rose bengal on the front face. Since a rose bengal tends [comparatively] to permeate the skin, said drug bearing body permeates a skin surface part a little. If a supersonic wave is turned to the skin and irradiated in this condition, in order that said cutaneous-absorption accelerator may be emitted in the skin and the barrier function of the skin may fall or disappear, a drug usually like the insulin which cannot be easily absorbed by the skin is absorbed in the skin.
[0123] In addition, the application to the therapy of the Kaposi sarcoma by athlete's foot, a viral bulla, psoriasis, scabies, skin carcinoma, and AIDS etc. is possible for the above-mentioned approach besides the therapy of a skin infectious disease.
[0124] [Diabetes-mellitus therapy] The drug bearing body which connotes an insulin is poured in into a blood vessel, and diabetes mellitus can be treated by destroying said drug bearing body and emitting an internal insulin to the inside of the body by [which is the need] turning a supersonic wave to the inside of the body, and by the way, irradiating it. In this case, it becomes possible to prescribe an insulin for the patient periodically by easy actuation by adjusting time amount, reinforcement, etc. which irradiate a supersonic wave.
[0125] Moreover, it is also possible to use the erythrocyte in blood as the above-mentioned drug bearing body. For example, an erythrocyte is separated out of blood and adhesion processing of Foto Phi Lynne who is the ultrasonic susceptibility matter after pouring in an insulin into each erythrocyte is carried out on the front face of the film of an erythrocyte.
[0126] Although it will not be destroyed during that period unless a supersonic wave is irradiated, since an erythrocyte has a life for about 100 days if blood transfusion etc. supplies by using an erythrocyte [finishing / this processing] as a patient's inside of the body, ultrasonic irradiation can be carried out from the outside of the body if needed, and an insulin can be emitted.
[0127] In this case, since a drug bearing body is constituted from an erythrocyte which is the construction material which is easy to suit the body, it becomes possible to control the rejection from the body.
[0128]
[Example] The example of an experiment which checks the effectiveness of this invention and which went to accumulate is explained. However, there is never nothing what limits this invention to this.
[0129] [Example of an experiment] The minute hollow sphere wrapped in albumin was made to contain at a rate of about 100 million pieces in 1ml of 5% human serum albumin in a beaker, and it divided into what performed processing by the rose bengal which is the ultrasonic susceptibility matter, and the thing which has not performed this processing.
[0130] The supersonic wave was irradiated for 30 seconds by 1MHz and 0.5 W/cm2 at the beaker containing each minute hollow sphere, and the number of a minute hollow sphere after an exposure was counted.
[0131] Although most minute hollow spheres coated with the rose bengal had broken, as for the unsettled thing, the configuration of 70% of number was still maintained.
[0132] Thus, the destructive effectiveness which was not acquired only with the mechanical energy of a supersonic wave was able to be acquired by existence of a rose bengal.
[0133] In addition, the same result was able to be obtained, even if it replaced with the rose bengal and used coloring matter, such as eosin.
[0134]
[Effect of the Invention] The ultrasonic susceptibility matter contained in a drug bearing body can be activated, and it is not necessary to destroy this drug bearing body, to make an internal drug emit efficiently, and to set up ultrasonic irradiation conditions finely in claims 1, 6, and 8 or

invention of 9, in that case by irradiating a supersonic wave in the object part in the living body at said drug bearing body which ****(ed) the drug.
[0135] In invention of claim 2, since the centrum was formed by **** which has predetermined thickness in a drug bearing body, it becomes possible to destroy drug support effectively in the part of this centrum.
[0136] In invention of claim 3, since said **** was made to contain, adhere or cover the ultrasonic susceptibility matter with a layer condition, it can have the effect of deterioration of the ultrasonic susceptibility matter on the whole ****.
[0137] In invention of claim 4, it becomes possible by making the ultrasonic susceptibility matter exist locally to destroy **** certainly.
[0138] In invention of claim 5, bleedoff of a drug can be made into a positive thing by having made thickness of said **** into within the limits of 0.001-50 micrometers.
[0139] In invention of claim 7, since said centrum was made to **** said drug in the condition of having made it ****ing with gas, it becomes possible to generate cavitation effectively.

[Translation done.]

* NOTICES *

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TECHNICAL FIELD

[Field of the Invention] About the technique of performing various kinds of therapies using supersonic vibration, especially, this invention controls administration of a drug and relates to the therapy promoting agent for emitting a drug effectively in a specific part in the living body using supersonic vibration.

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PRIOR ART

[Description of the Prior Art] Current cancer treatment is divided roughly into the two approaches of extinction of the cancer cell by extraction of the cancer organization by operation, or the anticancer drug object. Extraction of the cancer organization by operation can be performed, only when it is limited to the part where cancer is narrow or transition is not accepted, but on the other hand, the chemotherapy of cancer has a dramatically strong side effect, and the nausea by the medication of a large quantity, much renal dysfunction, and many impaired liver functions are accepted. And cancer reacts only to a high-concentration drug and the chemotherapy of cancer is not obtaining not much high **** results.
[0003] Many attempts are made to current and these problems. Although the approach called the missile therapy of an anticancer agent is an approach of applying the antibody combined selectively to a cancer cell as an anticancer agent, and making an anticancer agent acting on a cancer cell intensively, effectiveness sufficient for the moment is not acquired.
[0004] On the other hand, the inside of the body is injected with containment and it at drug bearing bodies, such as a capsule which consists an anticancer agent of specific matter, the method of prescribing the high-concentration anticancer agent by ** Li and the limited part for the patient for the husks is devised within the blood vessel near the cancer, and the effectiveness is proved in the experiment etc.
[0005] However, the method of tearing capsule husks efficiently in the above-mentioned approach is not yet established. Although various research of embedding a thermo sensor, a hydrogen ion exponent sensor, etc. which applied the polymer etc. to capsule husks, and inducing bleedoff of a drug on a certain temperature or hydrogen ion exponent conditions until now is done, it is dramatically difficult to set temperature and the conditions of a hydrogen ion exponent as arbitration near the tumor site.
[0006] Moreover, the approach to which destroy capsule husks with the impulse wave and ultrasonic energy from the outside, and an internal drug is made to emit was also considered.
[0007] For example, the approach of destroying the liposome which contains gas and a drug in a U.S. Pat. No. 5580575 description with a supersonic wave by the predetermined part of the patient inside of the body is indicated.
[0008] However, since powerful ultrasonic irradiation will be needed and the resonant frequency will be determined by the amount of the gas in a capsule in order to destroy capsules, such as liposome, mechanically only by oscillation of a supersonic wave in this way, it is difficult to destroy a capsule except the ultrasonic frequency.
[0009] Thus, in the activity of acoustical energy, although remarkable accuracy was required of the exposure setting out, in the tumor site, it was not easy to realize an exact ultrasonic frequency and reinforcement.

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EFFECT OF THE INVENTION

[Effect of the Invention] The ultrasonic susceptibility matter contained in a drug bearing body can be activated, and it is not necessary to destroy this drug bearing body, to make an internal drug emit efficiently, and to set up ultrasonic irradiation conditions finely in claims 1, 6, and 8 or invention of 9, in that case by irradiating a supersonic wave in the object part in the living body at said drug bearing body which ****(ed) the drug.
[0135] In invention of claim 2, since the centrum was formed by **** which has predetermined thickness in a drug bearing body, it becomes possible to destroy drug support effectively in the part of this centrum.
[0136] In invention of claim 3, since said **** was made to contain, adhere or cover the ultrasonic susceptibility matter with a layer condition, it can have the effect of deterioration of the ultrasonic susceptibility matter on the whole ****.
[0137] In invention of claim 4, it becomes possible by making the ultrasonic susceptibility matter exist locally to destroy **** certainly.
[0138] In invention of claim 5, bleedoff of a drug can be made into a positive thing by having made thickness of said **** into within the limits of 0.001-50 micrometers.
[0139] In invention of claim 7, since said centrum was made to **** said drug in the condition of having made it ****ing with gas, it becomes possible to generate cavitation effectively.

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TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] This invention makes it the technical problem to offer the drug support which makes it possible to realize high-concentration administration in said specific part of drugs, such as said anticancer agent, and its operation by destroying certainly drug bearing bodies, such as a capsule which ****(ed) drugs, such as an anticancer agent, by simple actuation using a supersonic wave in a specific part like the blood vessel of a cancer in-house, or a skin front face.

[Translation done.]

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MEANS

[Means for Solving the Problem] In order to solve the above-mentioned technical problem, in invention concerning claim 1 of this application, it carried out to making a drug bearing body contain the ultrasonic susceptibility matter.
[0012] In invention concerning claim 2, what has the centrum formed as said drug bearing body of **** which made the ultrasonic susceptibility matter contain, adhere or cover was adopted.
[0013] Said **** was made to contain, adhere or cover said ultrasonic susceptibility matter with a layer condition by invention concerning claim 3.
[0014] Said ultrasonic susceptibility matter was made to contain or adhere to said **** in the condition of having distributed massive, by invention concerning claim 4.
[0015] Invention concerning claim 5 prescribed the thickness of said **** to the range of 0.001-50 micrometers.
[0016] The drug was made to **** to the centrum formed of said **** in invention concerning claim 6.
[0017] Said centrum was made to **** said drug in the condition of having made it ****ing with gas, by invention concerning claim 7.
[0018] In invention concerning claim 8, the porphyrin derivative or the xanthene derivative was adopted as ultrasonic susceptibility matter.
[0019] In invention concerning claim 9, we decided to destroy said drug support by irradiating the supersonic wave of an output sentimental [square] 0.1-1000W /at a drug bearing body.
[0020]
[Embodiment of the Invention] This invention has the 1st description to make said ultrasonic susceptibility matter produce a chemical change or a physical change, destroy said drug bearing body, and make a drug emit, when said drug bearing body which ****(ed) the drug by including the ultrasonic susceptibility matter in the drug bearing body which the drug for a therapy is **** (ed) and can be conveyed to the object part is able to irradiate a supersonic wave in the object part.
[0021] Since destruction of this capsule is not influenced so much by the exposure conditions of a supersonic wave as compared with the approach to which destroy capsule husks only in the oscillating operation by the supersonic wave, and an internal drug is made to emit, this invention can adopt the ultrasonic energy of the comparatively large range that it is [square] sentimental 0.1-1000W /.
[0022] Therefore, like before, without performing conditioning of very difficult ultrasonic irradiation, in the object part in the living body, this drug bearing body can be destroyed effectively and a drug can be emitted also by supersonic waves other than the resonant frequency of a drug bearing body.
[0023] Moreover, this invention has the 2nd description to form a centrum and make this **** contain, adhere or cover the ultrasonic susceptibility matter with **** which has predetermined thickness in a drug bearing body. That is, while drug support can bear mechanical energies, such as a pressure, enough, it is designed by the structure which breaks easily according to the chemical change or physical change of said ultrasonic susceptibility matter.
[0024] The configuration of drug support is made into the shape of a capsule etc., it is massive,

and, specifically, the ultrasonic susceptibility matter is contained, adhered or covered by a layer condition or **** which constitutes a capsule. It becomes possible, when said ultrasonic susceptibility matter is in the layer condition to have the effect of deterioration of this ultrasonic susceptibility matter on said whole ****, and on the other hand, when said ultrasonic susceptibility matter is massive, it becomes possible by making this ultrasonic susceptibility matter exist in said **** locally to destroy this **** certainly. In addition, what was mixed to homogeneity may be used for the substrate ingredient which mentions the ultrasonic susceptibility matter later as an own component of drug support. In this case, while destruction of **** is performed uniformly, manufacture of drug support becomes easy.

[0025] Furthermore, although this invention is made to **** a drug to the centrum formed of said ****, it has the 3rd description for the gas of the specified quantity to be made to exist in said centrum with said drug. Although the class and amount of said gas are arbitrary so that it may mention later, it is desirable to be set up in 0.01 - 50% of range of the volume of said centrum. First, the component and structure of a drug bearing body concerning this invention are explained.

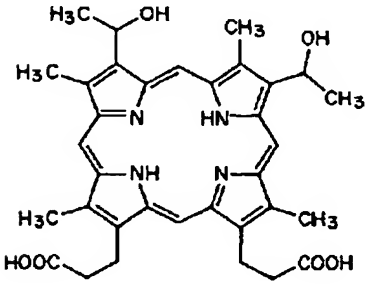
[0026] Although a "drug bearing body" is the carrier which the drug for a therapy is ****(ed) and can be conveyed to the inside of the body or the object part of a body surface here and especially the configuration is not limited, the capsule configuration which has the centrum carried out by **** the external world and ** exception is desirable, in view of the ease of manufacture, a manufacturing cost, etc.

[0027] The magnitude of a drug bearing body is usually suitably set up in 0.01-100 micrometers. In less than 0.01 micrometers, it is excreted by the outside of the body and effectiveness becomes imperfection, and when larger than 100 micrometers, the danger of causing a blood-flow failure is in a blood vessel.

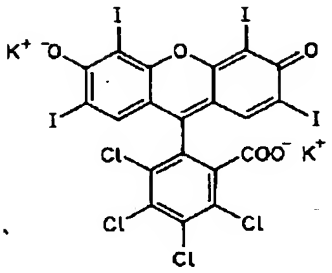
[0028] As a substrate ingredient which constitutes said drug bearing body, matter, such as various kinds of living body adaptation polymers, albumin, liposome, and sugar, can be used.

[0029] Moreover, improvement of the alternative translatability of an about [target group Oribe], water-soluble increment, acceleration of absorption, or relief of a side effect can also be aimed at by using the drug bearing body to which prodrug-ized qualification was performed. In this case, after attaining the object of said qualification in the inside of the body, it is restored to the original drug bearing body enzyme-wise or nonenzymatic, and it becomes possible to recover the susceptibility over a supersonic wave etc. The drug bearing body to which prodrug-ized qualification was performed is contained under the category of this invention. In addition, what performed prodrug-ized processing may be suitably used for the drug ****(ed) by the drug bearing body.

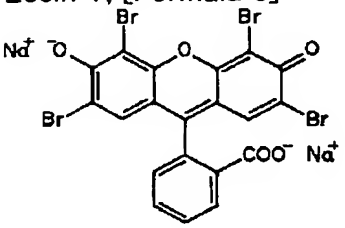
[0030] The "ultrasonic susceptibility matter" is matter which produces a certain change of changing structure of self [**** / producing a chemical change] to the matter of self [**** / activating through various devices], or others with the supersonic wave equipped with a predetermined frequency and reinforcement so that it may mention later. As said ultrasonic susceptibility matter, although a FURORE scene (fluorescein), merocyanine, etc. are mentioned, a porphyrin derivative or a xanthene derivative is desirable in respect of the compatibility to a toxic field and a toxic living body. It is the hematoporphyrin and [Formula 1] which specifically have the structure expression shown below as said porphyrin derivative or a xanthene derivative.



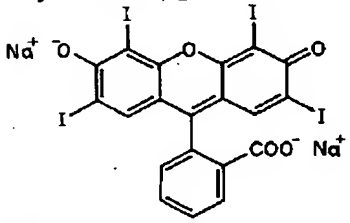
A rose bengal, [Formula 2]



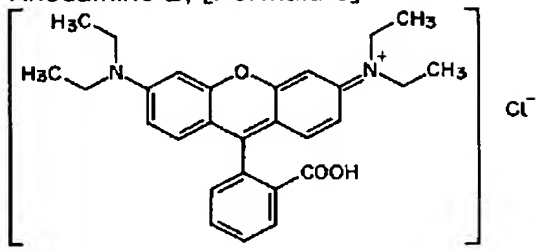
Eosin Y, [Formula 3]



Erythrosine, [Formula 4]



Rhodamine B, [Formula 5]



**********.

[0031] And although the lump of a drug 2 and the ultrasonic susceptibility matter 3 be distribute at suitable spacing in the drug bearing body 1 of an infinite form as structure of a drug bearing body so that it may be indicate by drawing 1 , it be desirable to form a centrum and to make this **** contain , adhere or cover the above-mentioned ultrasonic susceptibility matter with **** which have predetermined thickness in the drug bearing body itself at the point which enable effective destruction of this drug support .

[0032] As long as said centrum is formed in the interior of a drug bearing body, especially the number may not be limited, may be one, or may be plural. Moreover, although especially the formation part is not limited, either, in order to emit a drug good, it is desirable to be formed in the surface section of a drug bearing body. In addition, making the configuration of a drug bearing body itself into the shape of a capsule constituted by the layer of **** which has said predetermined thickness is also included in the range of this invention.

[0033] Here, the thickness of said **** is usually determined within the limits of 0.001-50 micrometers. When the thickness of **** is set to less than 0.001 micrometers, **** becomes destroyed [tend] by the impact, and before arriving at the object part in the living body, a possibility that said **** may be destroyed and an internal drug may flow out is. On the other hand, if set to 50 micrometers or more, even if it will become difficult to destroy said **** also according to an operation of the ultrasonic susceptibility matter and a part of **** will be

destroyed, the amount of husks wall which cannot be destroyed will remain, and there will be a possibility of barring bleedoff of a drug.
[0034] When it makes it face to contain the ultrasonic susceptibility matter to a drug bearing body and this drug bearing body is equipped with husks box-frame construction, it is desirable to make said ultrasonic susceptibility matter contain, adhere or cover in this ****.
[0035] The layer of the ultrasonic susceptibility matter 3 may specifically be covered to the outside surface of **** 1a, as shown in drawing 2 R> 2 (a), or the inner skin of **** 1a may be coated like drawing 2 (b), and you may make it exist in the interior of **** 1a in the state of a layer like drawing 2 (c). In addition, the layer of the ultrasonic susceptibility matter 3 does not need to be a continuous layer system as shown in drawing 2 , and it is not necessary to make it exist in **** 1a and concentric circular.
[0036] Moreover, the ultrasonic susceptibility matter 3 may be made to contain or adhere to **** 1a in the condition of having made it distributing massive. That is, as shown in drawing 3 (a) and drawing 3 (b), the lump of the ultrasonic susceptibility matter 3 may be made to adhere to the outside surface and internal surface of said **** 1a, and you may distribute suitably for the interior of said **** 1a like drawing 3 (c). In this case, each lump may project in part from ****1a, and does not need to project.
[0037] And as shown in drawing 3 (d), it is good also as structure which the lump of the ultrasonic susceptibility matter 3 penetrates **** 1a, and the part exposes to the external world and a building envelope, respectively. If it is when shown in drawing 3 , you may be distributing to homogeneity at said **** 1a, and the lump of said ultrasonic susceptibility matter 3 may be distributed for roughness and fineness. Moreover, especially each lump's configuration may not be limited and may be various configurations other than a globular form.
[0038] In addition, in drawing 2 and drawing 3 , 4 is the centrum formed of **** 1a, and the drug of a predetermined class is ****(ed) by this centrum.
[0039] Next, it explains, referring to drawing 4 about the operation of the drug bearing body mentioned above.
[0040] The above-mentioned drug bearing body which ****(ed) the drug of a predetermined class is injected into the inside of the body by the ion TOFORESHISU technique using the drug bearing body which used medication implements, such as a syringe, or was ionized by internal use, dermal administration, or the special approach etc.
[0041] And when the activity of a catheter or an endoscope is possible, the ultrasonic generating component for a therapy is introduced into the inside of the body of installation and a patient at the head of a catheter or an endoscope, and is made to reach the affected part.
[0042] Drawing 4 (a) and drawing 4 (b) are the sectional views showing the installation mode of the ultrasonic generating component used in operation of this invention, respectively, and drawing 4 (a) shows structure when drawing 4 (b) attaches the structure at the time of attaching an ultrasonic generating component in the point of an endoscope in the point of a catheter again.

[0043] In the mode shown in drawing 4 (a), the very small central canal 6 including wiring for operating the optical fiber and the supersonic vibration component mentioned later which is not illustrated is installed in the interior of the capillary 5 which constitutes an endoscope, and the 1st cylindrical shape-like supersonic vibration component 9 and the 2nd supersonic vibration component 10 which have a centrum in the direction of an axis at the head of a capillary 5 are arranged in concentric circular. As a supersonic vibration component, what attached the electrode in both sides of a piezoelectric device, for example is mentioned, and a supersonic wave is emitted by impressing the electrical signal of an ultrasonic frequency to this inter-electrode one in this case. 8 is the core section for transmitting to the optical fiber which does not illustrate an external image, and is embedded at said centrum. Moreover, the gap of a capillary 5 and the very small central canal 6 is made into the drug supply way 7, and is connected with the breakthrough 11 which carries out opening at suitable spacing for the peripheral surface by the side of the head of a capillary 5.
[0044] And each frequency characteristics differ, by controlling both actuation, two kinds of frequencies are mixed and said 1st supersonic vibration component 9 and the 2nd supersonic

vibration component 10 are oscillated in the direction (the direction of an arrow head) where the shaft orientations of an endoscope are vertical. Thus, it emanates combining two or more kinds of supersonic waves because the destructive effectiveness of direction of a complicated supersonic-wave wave of a drug bearing body improves. In addition, the 1st [which has the above-mentioned structure], and 2nd supersonic vibration components may be attached at the head of a catheter. On the other hand, the laminating is carried out in the direction of an axis of a catheter, both the 1st ultrasonic oscillation component 9 and 2nd ultrasonic oscillation component 10 from which frequency characteristics differ in the mode shown in drawing 4 R> 4 (b) being used as the shape of a cylindrical shape of a solid.
[0045] Therefore, the supersonic wave which has two kinds of frequencies in the direction of an axis of a catheter (the direction of an arrow head) is oscillated by controlling both actuation.
[0046] In addition, the 1st [which has the above-mentioned structure], and 2nd supersonic vibration components may be attached at the head of an endoscope.
[0047] Now, a drug bearing body is turned and emitted to the affected part from the drug supply way 7 through opening 11 after checking that the head of an endoscope or a catheter has arrived at the affected part organization. it — simultaneously — or after predetermined time progress — super- — if the 1st and 2nd supersonic vibration components are operated, the supersonic wave with which frequencies differ will be emitted to the affected part, and will destroy the drug bearing body which exists during an affected part organization. Therefore, the drug in a drug bearing body is limited and prescribed for the patient only around an affected part organization part.
[0048] It is desirable to choose a device in consideration of the relative position of the affected part to said endoscope or catheter, so that the exposure of a suitable supersonic wave may be obtained. Moreover, the diameter of said endoscope or a catheter can use the thing of the range of about 5cm from 1mm, choosing it suitably.
[0049] In addition, three or more sorts of above-mentioned ultrasonic oscillation components may be attached. In that case, since a still more complicated ultrasonic wave is generable, the destructive effectiveness of a drug bearing body improves further. When it is the configuration which a drug bearing body is easy to be destroyed, the supersonic vibration component of 1 may be used.
[0050] two or more sonicators for a therapy which carried out the laminating of the 1st supersonic vibration component 9 which have the property same with having describe above to the crevice of the base 12 which consist of flexible synthetic resin etc. as show in drawing 5 , and the 2nd supersonic vibration component 10 , and have arrange them on the other hand when neither a catheter nor an endoscope can be use be preferably lay on the skin corresponding to the affected part , and a supersonic wave be turn to the affected part (the direction of an arrow head) , and be irradiate . It is desirable to prepare two or more laminated material of a supersonic vibration component in a base 12 so that it may illustrate. Since a base 12 can curve according to the configuration of a patient's body, it can centralize a supersonic wave on the affected part. The diameter of said 1st and 2nd supersonic vibration components is usually suitably set up in 5cm - 10cm. In addition, said 1st supersonic vibration component 9 and the 2nd supersonic vibration component 10 have it, in order that the direction which consists of oscillation ingredients with flexibility like a fluorine compound may maintain the flexibility of the whole equipment and may secure the adhesion to the skin etc. [desirable]
[0051] And the ultrasonic energy concentrated on the affected part destroys the drug bearing body which exists there, and emits an internal drug to the affected part.
[0052] Thus, in this invention, destruction becomes possible [destroying the difficult drug bearing body easily, setting at least inside the desired body, and controlling bleedoff of a drug] only ultrasonically by including the ultrasonic susceptibility matter in a drug bearing body.
[0053] In addition, since a drug bearing body can be made to accumulate on an affected part organization when matter, such as an antibody selectively combined with affected part organizations, such as a cancer cell, a thrombus, an organ, and a blood vessel that carried out arteriosclerosis, is included in the substrate ingredient of a drug bearing body, it becomes possible to destroy the drug bearing body accumulated on this affected part organization using a

supersonic wave, and to medicate high concentration with a drug locally.
[0054] Next, the conditions of the supersonic wave used in this invention are explained.
[0055] The output of the supersonic wave irradiated for destruction of the drug bearing body concerning this invention is suitably set up in the range sentimental [square] 0.1-1000W /. If the outputs of a supersonic wave are two or less 0.1 W/cm, only the energy which activates the ultrasonic susceptibility matter runs short, and since there is too much heat release when it becomes two or more 1000 W/cm, a damage will be given to a living body.
[0056] Moreover, although the frequency of a supersonic wave is suitably set up in 10kHz - 100MHz, the range of 20kHz - 10MHz is desirable especially. According to the supersonic wave of this frequency band, it becomes possible to generate the cavitation later mentioned with comparatively low energy, and to destroy a drug bearing body efficiently.
[0057] And as mentioned above, it is also possible to activate the ultrasonic susceptibility matter more efficiently by combining two or more frequencies, and to destroy a drug bearing body. For example, while irradiating the supersonic wave of a fixed frequency, intermittently, this is changing to a different frequency, generating of the cavitation mentioned later can be reinforced intentionally, or it controls, and a drug bearing body can be destroyed or disassembled.
[0058] When the example was given, while carrying out continuous irradiation of the supersonic wave to the affected part by 100kHz, much more destructive effectiveness was acquired by changing to the frequency of 270kHz in the shape of a short-time (0.001sec-10sec) pulse. The same effectiveness is expected, even if it is fixed within the limits and carries out continuation adjustable [of the frequency of a supersonic wave]. This phenomenon is considered that destructive power increased by stopping resonance motion of a drug bearing body temporarily.
[0059] Here, the device of destruction of a drug bearing body is explained.
[0060] If the ultrasonic energy beyond the value which is among a liquid is generally given, the minute air ball called cavitation will occur. It is related with the generating mechanism of cavitation. For example Robert E.Apfel:"Sonic effervescence:tutorial on acoustic cavitation", Journal of Acoustic Society of America 101(3):1227-1237 and March 1997, Atchley A, and Crum L:"Ultrasound-Its chemical, Physical and biological effects:Acoustic cavitation and bubble dynamics", and Ed Although indicated by Suslick K, pp 1-64, 1988 VCH Publishers, and New York, it explains briefly [below]. Cavitation is that the gas which has melted into the water solution serves as air bubbles, or the very very small bubble which had already existed repeats an oscillation or amplification, and a cutback, and turns into air bubbles under a certain acoustical oscillation.
[0061] And if this cavitation becomes the magnitude of extent which cannot maintain that magnitude, it will collapse, but since this breaking takes place rapidly, it is known that various energy will occur locally then.
[0062] That is, in the case of breaking of the above-mentioned cavitation, the hot spot of 6000 - 7000 degrees is formed in the core, and various energy other than mechanical energies, such as an oscillation, such as electromagnetic waves, such as a visible ray and ultraviolet rays, heat, plasma, electromagnetic field, a shock wave, a free radical, and heat, is considered to generate locally.
[0063] It is thought that it activates with the above-mentioned various energy produced in the case of cavitation breaking, or the ultrasonic susceptibility matter in this invention produces a chemical change, or changes structure.
[0064] For example, the rose bengal which is one of the ultrasonic susceptibility matter in this invention is excited and activated by light or ultraviolet rays with a wavelength of 530nm. Therefore, it is thought that activation of a rose bengal is caused by the ultraviolet rays generated in the case of cavitation breaking.
[0065] By the way, in the liquid with which the ultrasonic susceptibility matter exists, it is known that the threshold of the ultrasonic energy for cavitation generating will become low. Therefore, the ultrasonic susceptibility matter contained in the drug bearing body does so the effectiveness of activation etc. acting as itself and destroying a drug bearing body with the energy which carried out induction of the cavitation generating near the drug bearing body selectively, and was produced by breaking of cavitation.

[0066] Also when the minute bubble exists in a liquid on the other hand, it is known that the threshold of the ultrasonic energy for cavitation generating will become low.
[0067] Therefore, by making the gas of the specified quantity exist in drug support, cavitation is effectively generated at the time of ultrasonic irradiation, and the energy produced in the case of this cavitation breaking can be used effective in destruction of drug support. Although the class and amount of said gas are arbitrary, as for the amount, it is desirable to be set up in 0.01 - 50% of range of the volume of the centrum in a drug bearing body. If the cause of the generating of cavitation cannot be effectively carried out to the amount of said gas being said less than 0.01% of centrum volume and the amount of said gas exceeds said 50% of centrum volume, the reinforcement of a drug bearing body will not be maintained and the amount of the medicine conveyed will be restricted until it arrives at the object part.
[0068] In addition, it is also possible to use for the therapy of an affected part organization directly using various energy, such as electromagnetic waves, such as a visible ray produced in the case of breaking of cavitation and ultraviolet rays, heat, plasma, electromagnetic field, a shock wave, a free radical, and heat.
[0069] For example, by generating a supersonic wave near the affected part organization, the ultraviolet rays which are usually absorbed by the skin and do not reach the inside of the body are generated near the affected part tissue in the living body by breaking of the cavitation originating in a supersonic wave, and it becomes possible to treat the affected part by the germicidal action.
[0070] That is, cavitation is generated with a supersonic wave in a body, and the approach of treating the affected part with the energy produced at the time of this breaking can be enforced.

[0071] Since according to this approach energy, such as ultraviolet rays, is generated free in all parts in the living body and the affected part is treated by this, it is not necessary to take into consideration the effect by the side effect of a proper to medication.
[0072] This invention can be carried out with a gestalt which is described below.
[0073] [Cancer treatment] The intravenous injection of what coated the outside surface of this capsule with a package and the ultrasonic susceptibility matter for the cisplatin which is an anticancer agent by the capsule of a polymer is given. It is toxicity even if the intravenous injection of said capsule is given, since cisplatin is covered by the polymer.

[Translation done.]

* NOTICES *

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2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

OPERATION

There is (no side effect) and the inside of blood is only flowed.
[0074] However, if a supersonic wave is irradiated while said capsule is flowing the inside of the blood vessel under cancer organization, the ultrasonic susceptibility matter on said front face of a capsule will be activated, the capsule which has wrapped cisplatin will be disassembled, and cisplatin will be emitted by high concentration all over this organization.
[0075] Therefore, while administration of the high-concentration anticancer agent in the limited part in which cancer is located is attained, a normal cellular structure becomes possible [escaping the strong toxicity of cisplatin].
[0076] As for this approach, effectiveness is acquired by especially diseases in which many blood vessels exist, such as liver cancer and a brain tumor. As the exposure approach of a supersonic wave, a neoplasm part can be irradiated from the front face of the skin, or a direct supersonic wave can also be irradiated in a cancer organization during a laparotomy.
[0077] Moreover, it is also possible to an endoscope to irradiate a supersonic wave for an ultrasonic component from the interior of installation and the body, and a direct supersonic wave can also be irradiated from the inside cavity of the interior of stomach, or the large intestine in that case at colon cancer etc.
[0078] According to a case, a suitable path is chosen from various roots, such as impregnation, dermal administration, etc. to the direct affected part, via the absorption from the intestinal tract according [the route of administration of the above-mentioned capsule] to internal use besides an intravenous injection, and a lymphatic duct.
[0079] By the way, since Foto Phi Lynne herself has the compatibility over a cancer cell when Foto Phi Lynne is used as the above-mentioned ultrasonic susceptibility matter, it concentrates on a cancer organization and the above-mentioned capsule containing cisplatin is accumulated in high concentration.
[0080] And it becomes possible by irradiating a supersonic wave in this condition to prescribe cisplatin for the patient further during a cancer organization at high concentration.
[0081] In addition, since Foto Phi Lynne also has the property which produces a killer cell operation when it activates with a supersonic wave, in this case, it combines with cisplatin and an anticancer operation is reinforced in multiplication.
[0082] Moreover, in the case of the cancer and vesical cancer which were transferred to intraperitoneal, direct intraperitoneal is injected with the capsule which connotes an anticancer agent, and how to turn a supersonic wave to the whole abdominal cavity, and irradiate it from a skin front face, can be considered after that. The case of vesical cancer can make said capsule full [in a bladder] from an urethra, and vesical cancer can be treated by irradiating a supersonic wave from the skin front face of the hypogastrium. While irradiating the supersonic wave for a therapy in these cases, it has the advantage that the bleedoff condition of a drug is observable with the supersonic wave for a diagnosis.
[0083] [Thrombolytic treatment] The thrombolytic agent is used as a remedy of myocardial infarction or cerebral infarction. However, in order to dissolve a thrombus as early as possible, when a medicine is prescribed for the patient so much, there is risk of being hard coming to solidify blood conversely and causing many bleeding.

[0084] Then, it injects with a package and this in a blood vessel by the capsule of the living body adaptation polymer which contains the ultrasonic susceptibility matter for thrombolytic agents, such as urokinase, or the product made from albumin. In the usual condition, since it is not destroyed, this capsule does not cause a solvent action within a blood vessel.
[0085] And if said capsule arrives at the part to which thrombuses, such as a peripheral vessel of a coronary artery, exist, for example in the case of myocardial infarction, by irradiating a supersonic wave from the outside of the body or the inside of the body using equipment which was described above, said capsule will be destroyed and a thrombolytic agent will be locally emitted by high concentration.
[0086] specifically, it is shown in drawing 6 — as — up to near the thrombus — the catheter with an ultrasonic radiator or endoscope of drawing 4 — the inside of a blood vessel — inserting — the capsule containing a thrombolytic agent — a thrombus — it emits from the upstream immediately and a supersonic wave is oscillated simultaneously. Said capsule is destroyed by operation of the ultrasonic susceptibility matter activated by the supersonic wave, and an internal thrombolytic agent is emitted to a thrombus part.
[0087] In addition, in case the capsule which was not destroyed ultrasonically flows and arrives at the affected part again, it is destroyed and used. And since said capsule is not destroyed until it reaches the affected part again, it does not become the factor of bleeding.
[0088] Moreover, when the matter or antibody which is specifically affinitive at a thrombus is beforehand given to the outside surface of a capsule, this capsule piles up a thrombus at high concentration. If a supersonic wave is irradiated to a thrombus part in the condition, it will become possible to destroy this capsule and to prescribe a thrombolytic agent for the patient effectively near the thrombus. It is reported that the matter which has compatibility in a thrombus is Lanza **** (Circulation, 1995, 92.Suppl I:1-260).
[0089] By doing in this way, thrombolytic treatment becomes possible efficiently, without causing side effects, such as bleeding.
[0090] [Blood vessel therapy] When arteriosclerosis etc. becomes a cause and the vasoconstriction happens, the operation therapy which a blood vessel lumen is extended [therapy] with a balloon catheter in recent years, and makes the flow of blood resume is performed briskly.
[0091] Moreover, after the above-mentioned operation, again, a therapy which is fixed where a blood vessel lumen is extended by the metal stent is also briskly performed so that the vasoconstriction may not occur.
[0092] However, a certain amount of breakage is done to the wall of a blood vessel in any case. That a carrier beam blood vessel organization should recover a blood vessel for breakage in the original condition, although restoration accompanied by growth of a blood vessel organization is performed, the case where too much restoration takes place in this restoration process, and the restenosis of a blood vessel is started goes up to 50% or more, and it considers as the fault of this therapy.
[0093] Then, the thing in which the drug bearing body which ****(ed) Foto Phi Lynne inside was made to mix as construction material of balun is adopted, the balloon catheter which located the ultrasonic generating component in the core is inserted into a blood vessel, balun is expanded in the object part, and it is made to stick to a blood vessel wall, as shown in drawing 7 .
[0094] ** by which the drug bearing body located in the part which touches the blood vessel wall of said balun if a supersonic wave is perpendicularly generated with the axis of said catheter in this condition is destroyed, and internal Foto Phi Lynne is directly poured in into a blood vessel wall.
[0095] Since FOTOFI Lynne has the property which checks the restoration process of a blood vessel organization to some extent when it activates ultrasonically, by balun, she becomes possible [controlling too much restoration of a carrier beam blood vessel wall] about breakage, and can prevent the restenosis.
[0096] In the gestalt of this operation, Foto Phi Lynne is ****(ed) in the drug bearing body as a drug for an affected part therapy, and although the ultrasonic susceptibility matter for this bearing body destruction contained in a drug bearing body is made into arbitration, Foto Phi

Lynne may be used as this ultrasonic susceptibility matter.
[0097] In addition, as a drug for an affected part therapy which can be used under a blood vessel therapy, the gene with which a blood vessel wall is medicated, heparin, the radioactive substance, etc. are mentioned.
[0098] [Activity as a hemostat] To hepatic carcinoma, ethanol is poured in into the nutrition blood vessel of current and a cancer organization, breakage is done to the wall of this blood vessel, a thrombus is made artificially, and this blood vessel is closed, or the liquid of a specific class is poured in, and the cure which prevents growth of a cancer cell by blocking a blood vessel etc. is performed.
[0099] Instead, by activating with a supersonic wave, the drug bearing body containing a rose bengal which demonstrates the operation as a blood vessel wall breakage agent, and this pour in simultaneously independently the drug bearing body containing a thrombin which has the operation as coagulant into a blood vessel, and adopt the approach of irradiating a supersonic wave in the affected part.
[0100] With the gestalt of this operation, the rose bengal is ****(ed) in the drug bearing body as a drug for an affected part therapy. And a rose bengal may be used although the ultrasonic susceptibility matter for this bearing body destruction contained in both the drug bearing body is arbitrary.
[0101] In this approach, although said drug bearing body is destroyed by the supersonic wave and the rose bengal of that interior is emitted in the affected part, in that case, the rose bengal itself is activated by the supersonic wave, breakage is done to a blood vessel wall, and a thrombus is formed.
[0102] And the thrombin which could come, simultaneously was emitted from the separate drug bearing body makes blood solidify. Therefore, the blood flow in the affected part is stopped.
[0103] Thus, the synergistic effect as a hemostat can be acquired by combining two sorts of drug bearing bodies.
[0104] Besides the therapy of hepatic carcinoma, the above-mentioned approach is suitable for the hemostasis of the organ bleeding by the traffic accident with which he was hardly able to deal until now.
[0105] [Percutaneous absorption of a drug] About the dermal administration of the drug which used the supersonic wave together, it is just already going to be known. For example, it has many detailed bores and the processor which consists of a disc-like board with which the liquid was contained inside is developed so that it may be indicated by the description of Japanese Patent Application No. No. 166334 [nine to]. In this equipment, it is possible efficiently by making a detailed hole on the surface of the skin using a cavitation generating phenomenon to perform administration of a drug or extraction of body fluid, without being accompanied by the pain.
[0106] With the gestalt of this operation, the drug bearing body which contained the ultrasonic susceptibility matter in said bore in the above-mentioned processor is arranged.
[0107] Hereafter, it explains with reference to drawing 8 .
[0108] In this example, the dermal administration equipment 13 of a drug is constituted from a film which consists of a comparatively thin synthetic-resin ingredient of the range of 1 micrometer - 1cm etc., and the circular space 14 is formed in the interior.
[0109] Two or more bores 16 which are outside open for free passage from the circular space 14 are formed in the bottom side film 15 of dermal administration equipment 13. The diameter of a bore 16 can be made into the range of 0.1mum-3mm. In addition, although the bore 16 is distributed over homogeneity in the example of drawing 8 , in it, it may be prepared in roughness and fineness if needed. Moreover, unfairness, such as not only a circle but stellate, a polygon, etc., is sufficient as the cross-section configuration of a bore 16. The consistency of a bore 16 can be made into 1 per 1 square centimeters to 1 million range.
[0110] On the other hand, the supersonic vibration component 18 is attached in the upside film 17 of dermal administration equipment 13. Although this supersonic vibration component 18 may be formed in one with dermal administration equipment 13, you may make it force this on the upside film 17 of dermal administration equipment 13 as a member which became independent independently.

[0111] It faces using the dermal administration equipment 13 of a drug, the drug bearing body 19 is arranged in a bore 16, and the circular space 14 and the **** space 20 of the drug bearing body 19 interior are filled with the liquid drug 21.
[0112] And the bottom side film 15 of dermal administration equipment 13 is stuck by pressure on the surface of the skin, a driving signal is supplied to the supersonic vibration component 18, and a supersonic wave is generated. Then, while the drug bearing body 19 is destroyed and a bore 16 is opened for traffic, cavitation occurs in the liquid drug 21 in the circular space 14, the liquid flow of the high speed produced at the time of breaking of this cavitation passes a bore 16, the skin is reached, and a detailed hole is formed in that front face. The liquid drug 21 is absorbed by the inside of the body through this hole.
[0113] By doing in this way, even when a bore 16 is comparatively large, a liquid drug does not flow out of a bore 16 at the time of storage of dermal administration equipment 13. On the other hand, since the drug bearing body 19 is destroyed by the supersonic wave, a bore 16 can be made certainly opened for traffic in the case of an activity.
[0114] Moreover, since the ultrasonic susceptibility matter in the drug bearing body 19 reduces the threshold of cavitation generating, cavitation can be generated in the liquid drug 21 with low ultrasonic energy. It becomes possible to lessen by this ultrasonic energy irradiated by the skin, and a possibility of having an adverse effect on the skin decreases.
[0115] As drugs prescribed for the patient into the skin using this equipment, there is an antiallergic agent, an insulin, various hormone, an anticancer agent, an anti-inflammatory agent, an anesthetic, an anticoagulant (heparin, urokinase), an antibiotic, various vitamins, a steroid, a pressure-up agent, a hypotensor, a psychotropic, hair growing, or a depilatory.
[0116] [Infectious disease therapy] Although the sterilization disinfection effectiveness by UV light is known well, UV light is [only being used for disinfection of front faces, such as a medical device, and] in atmospheric air chiefly, in order that the permeability in the inside of a liquid may be very bad and may decline promptly.
[0117] By the way, it is known that sirloin BENGARU which is the ultrasonic susceptibility matter also has the operation which reduces the threshold of cavitation generating by the supersonic wave.
[0118] Then, this property can be used and a supersonic wave can be used for the therapy of the infectious disease outside the inside of the body at the therapy of the infectious disease in the inside of the body.
[0119] Namely, in the infectious disease therapy in the inside of the body, if the bearing body containing a rose bengal is made to invade to the depths of the affected part by injection etc. and a supersonic wave is irradiated towards the affected part in the condition, as cavitation occurred and mentioned already with comparatively low ultrasonic energy on these outskirts of a bearing body, UV light will occur at the time of the breaking.
[0120] Therefore, UV light is irradiated from point-blank range at the affected part in the living body, and since it becomes possible to sterilize, it becomes possible to apply to the therapy of an infectious disease.
[0121] Moreover, since various antibiotics do not need to be used for this approach, it has the advantage of not making resistant bacteria.
[0122] Next, in the case of a skin infectious disease, it is the drug bearing body which ****(ed) the cutaneous-absorption accelerator, and it applies to a skin front face what covered the rose bengal on the front face. Since a rose bengal tends [comparatively] to permeate the skin, said drug bearing body permeates a skin surface part a little. If a supersonic wave is turned to the skin and irradiated in this condition, in order that said cutaneous-absorption accelerator may be emitted in the skin and the barrier function of the skin may fall or disappear, a drug usually like the insulin which cannot be easily absorbed by the skin is absorbed in the skin.
[0123] In addition, the application to the therapy of the Kaposi sarcoma by athlete's foot, a viral bulla, psoriasis, scabies, skin carcinoma, and AIDS etc. is possible for the above-mentioned approach besides the therapy of a skin infectious disease.
[0124] [Diabetes-mellitus therapy] The drug bearing body which connotes an insulin is poured in into a blood vessel, and diabetes mellitus can be treated by destroying said drug bearing body

and emitting an internal insulin to the inside of the body by [which is the need] turning a supersonic wave to the inside of the body, and by the way, irradiating it. In this case, it becomes possible to prescribe an insulin for the patient periodically by easy actuation by adjusting time amount, reinforcement, etc. which irradiate a supersonic wave.

[0125] Moreover, it is also possible to use the erythrocyte in blood as the above-mentioned drug bearing body. For example, an erythrocyte is separated out of blood and adhesion processing of Foto Phi Lynne who is the ultrasonic susceptibility matter after pouring in an insulin into each erythrocyte is carried out on the front face of the film of an erythrocyte.

[0126] Although it will not be destroyed during that period unless a supersonic wave is irradiated, since an erythrocyte has a life for about 100 days if blood transfusion etc. supplies by using an erythrocyte [finishing / this processing] as a patient's inside of the body, ultrasonic irradiation can be carried out from the outside of the body if needed, and an insulin can be emitted.

[0127] In this case, since a drug bearing body is constituted from an erythrocyte which is the construction material which is easy to suit the body, it becomes possible to control the rejection from the body.

[Translation done.]

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EXAMPLE

[Example] The example of an experiment which checks the effectiveness of this invention and which went to accumulate is explained. However, there is never nothing what limits this invention to this.
[0129] [Example of an experiment] The minute hollow sphere wrapped in albumin was made to contain at a rate of about 100 million pieces in 1ml of 5% human serum albumin in a beaker, and it divided into what performed processing by the rose bengal which is the ultrasonic susceptibility matter, and the thing which has not performed this processing.
[0130] The supersonic wave was irradiated for 30 seconds by 1MHz and 0.5 W/cm2 at the beaker containing each minute hollow sphere, and the number of a minute hollow sphere after an exposure was counted.
[0131] Although most minute hollow spheres coated with the rose bengal had broken, as for the unsettled thing, the configuration of 70% of number was still maintained.
[0132] Thus, the destructive effectiveness which was not acquired only with the mechanical energy of a supersonic wave was able to be acquired by existence of a rose bengal.
[0133] In addition, the same result was able to be obtained, even if it replaced with the rose bengal and used coloring matter, such as eosin.

[Translation done.]

* NOTICES *

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2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]
[Drawing 1] Cross-section structural drawing to show an example of the gestalt of operation of a drug bearing body.
[Drawing 2] Cross-section structural drawing to show other examples of the gestalt of operation of a drug bearing body.
[Drawing 3] Cross-section structural drawing to show an example of further others of the gestalt of operation of a drug bearing body.
[Drawing 4] The sectional view showing the installation mode of the ultrasonic generating component used in operation of this invention.
[Drawing 5] The sectional view showing one mode of the sonicator for a therapy.
[Drawing 6] The expanded sectional view for explaining the case where the drug bearing body of this invention is applied to thrombolytic treatment.
[Drawing 7] The expanded sectional view for explaining the case where the drug bearing body of this invention is applied to a blood vessel therapy
[Drawing 8] The sectional view of the dermal administration equipment adapting the drug bearing body of this invention
[Description of Notations]
1 Drug Bearing Body
1a ****
2 Drug
3 Ultrasonic Susceptibility Matter
4 Centrum
5 Capillary
6 Very Small Central Canal
7 Drug Supply Pipe
8 Core Section
9 1st Supersonic Vibration Component
10 2nd Supersonic Vibration Component
11 Opening
12 Base
13 Dermal Administration Equipment
14 Circular Space
15 Bottom Side Film
16 Bore
17 Upside Film
18 Supersonic Vibration Component
19 Drug Bearing Body
20 **** Space
21 Liquid Drug

[Translation done.]

* NOTICES *

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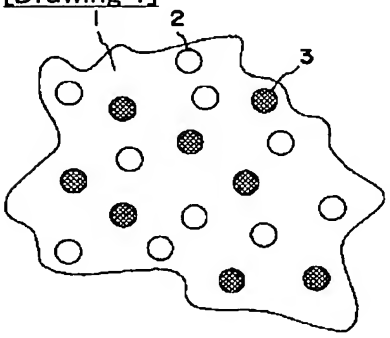
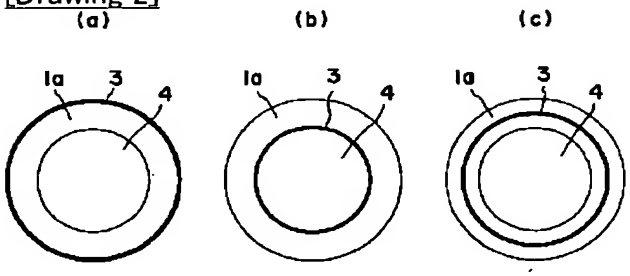
DRAWINGS

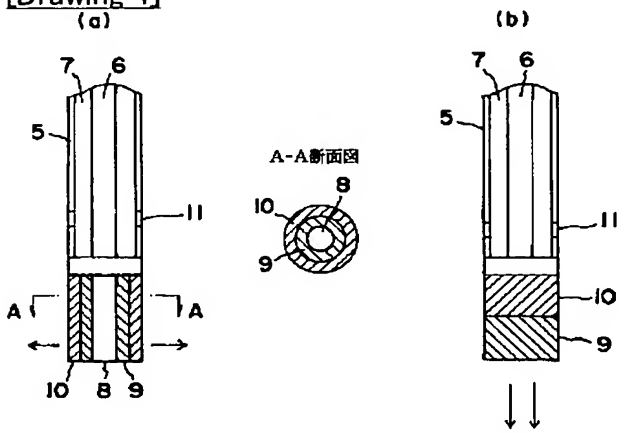
[Drawing 1]



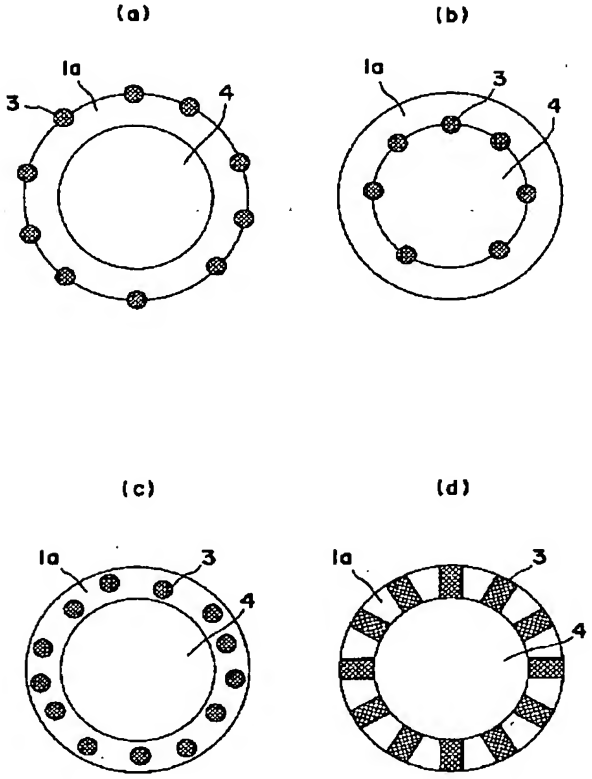
[Drawing 2]



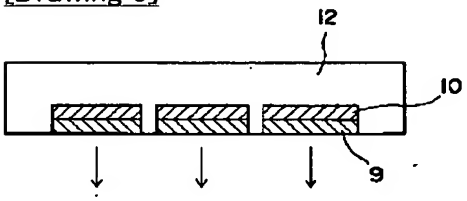
[Drawing 4]



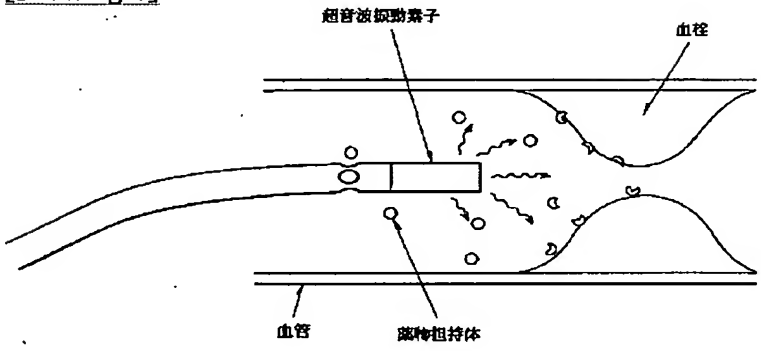
[Drawing 3]



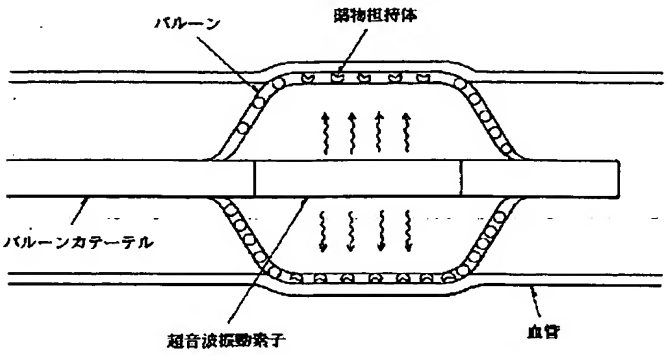
[Drawing 5]



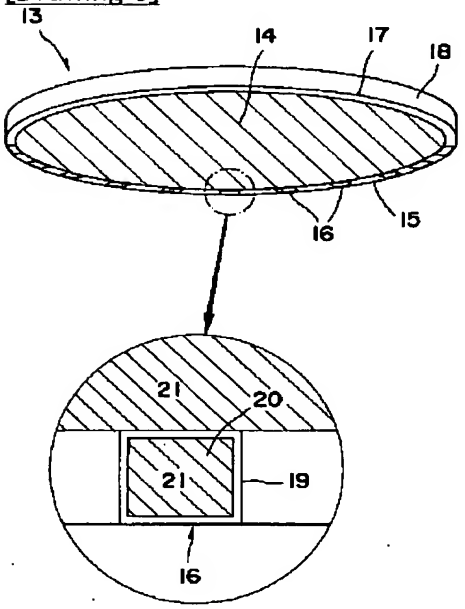
[Drawing 6]



[Drawing 7]



[Drawing 8]



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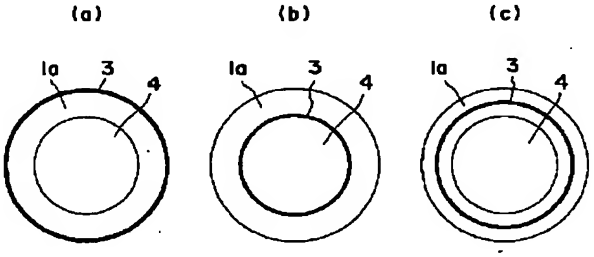
(54)【発明の名称】　薬物坦持体及びその使用方法

(57)【要約】

【課題】抗癌剤等の薬物を坦持したカプセル等の薬物坦持体を、癌組織内の血管或いは皮膚表面のような特定の部位において超音波を用いて確実に、かつ簡易な操作で破壊することにより、前記抗癌剤等の薬物の前記特定の部位における高濃度の投与を実現することを可能とする薬物担持体及びその使用方法を提供すること。

【解決手段】治療用薬物の坦持体に超音波感受性物質を含有させる。薬物坦持体としては、超音波感受性物質を含有、付着又は被覆させた殻壁によって形成された中空部を有するものが好ましく、その場合は、前記超音波感受性物質を層状態で前記殻壁に含有、付着又は被覆させるか、または、前記超音波感受性物質を塊状に分散した状態で前記殻壁に含有又は付着させる。



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【特許請求の範囲】
【請求項１】　超音波感受性物質を含む薬物坦持体
【請求項２】　超音波感受性物質を含有、付着又は被覆させた殻壁によって形成された中空部を有する請求項１記載の薬物坦持体
【請求項３】　前記超音波感受性物質が層状態で前記殻壁に含有、付着又は被覆されている請求項２記載の薬物坦持体。
【請求項４】　前記超音波感受性物質が塊状に分散した状態で前記殻壁に含有又は付着されている請求項２記載の薬物坦持体。
【請求項５】　前記殻壁の厚さが０．００１～５０μｍである請求項２乃至４のいずれかに記載の薬物坦持体。
【請求項６】　前記殻壁によって形成された中空部に薬物を坦持させたことを特徴とする請求項２乃至５のいずれかに記載の薬物坦持体。
【請求項７】　前記薬物をガスと併存させた状態で前記中空部に坦持させたことを特徴とする請求項６記載の薬物坦持体
【請求項８】　前記超音波感受性物質が、ポルフィリン誘導体又はキサンテン誘導体であることを特徴とする請求項１乃至７のいずれかに記載の薬物坦持体
【請求項９】　請求項１乃至８のいずれかに記載の薬物坦持体に０．１～１０００ワット／平方センチの出力の超音波を照射することにより前記薬物担持体を破壊することを特徴とする前記薬物坦持体の使用方法。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】本発明は、超音波振動を利用して各種の治療を行う技術に関し、特に、薬物の投与を制御し、体内の特定の部位において超音波振動を利用して薬物の放出を効果的に行うための治療促進物質に関する。
【０００２】
【従来の技術】現在の癌治療は、手術による癌組織の摘出又は抗癌薬物による癌細胞の死滅の二つの方法に大別される。手術による癌組織の摘出は、癌が狭い部位に限定され、又は、転移が認められない場合にしか行うことができず、一方、癌の化学療法は副作用が非常に強く、大量の薬物投与による吐き気、腎機能障害、肝機能障害が多く認められる。そして、癌は高濃度の薬物にしか反応せず、癌の化学療法はあまり高い治療成績をあげていない。
【０００３】現在、これらの問題に対して多くの試みがなされている。抗癌剤のミサイル療法と呼ばれる方法は、抗癌剤として癌細胞に選択的に結合する抗体を応用したものであり、癌細胞に集中的に抗癌剤を作用させる方法であるが、今のところ十分な効果は得られていない。
【０００４】一方、抗癌剤を特定の物質よりなるカプセル等の薬物坦持体に封じ込め、それを体内に注射して癌の近くの血管内でその殻を破り、限定された部位で高濃度の抗癌剤を投与する方法が考案され実験等でその効果が証明されている。

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【０００５】しかし、上記した方法においてカプセル殻を効率よく破る方法は未だ確立されていない。これまで、カプセル殻に、ポリマーなどを応用した温度センサー、ペーハーセンサー等を埋め込み、ある温度又はペーハー条件で薬物の放出を誘発する等の様々研究が行われているが、腫瘍部位近くで温度、ペーハーの条件を任意に設定することは非常に困難である。
【０００６】また、外部からの衝撃波や超音波エネルギーでカプセル殻を破壊して内部の薬物を放出させる方法も考えられた。
【０００７】例えば、米国特許第５５８０５７５号明細書には、ガス及び薬物を含むリポゾームを患者体内の所定部位で超音波により破壊する方法が記載されている。
【０００８】しかしながら、このように超音波の振動のみで機械的にリポゾーム等のカプセルを破壊するには、強力な超音波照射を必要とし、また、カプセル内のガスの量により、その共鳴周波数は決定されてしまうので、その超音波周波数以外ではカプセルを破壊することは難しい。
【０００９】このように、音響学的なエネルギーの使用においては、その照射設定にかなりの正確さが要求されるが、腫瘍部位において、正確な超音波周波数及び強度を実現することは容易でなかった。
【００１０】
【発明が解決しようとする課題】本発明は、抗癌剤等の薬物を坦持したカプセル等の薬物坦持体を、癌組織内の血管或いは皮膚表面のような特定の部位において超音波を用いて確実に、かつ簡易な操作で破壊することにより、前記抗癌剤等の薬物の前記特定の部位における高濃度の投与を実現することを可能とする薬物担持体及びその使用方法を提供することをその課題とする。
【００１１】
【課題を解決するための手段】上記課題を解決するために、本願の請求項１に係る発明では、薬物坦持体に超音波感受性物質を含有させることとした。
【００１２】請求項２に係る発明では、前記薬物坦持体として、超音波感受性物質を含有、付着又は被覆させた殻壁によって形成された中空部を有するものを採用した。
【００１３】請求項３に係る発明では、前記超音波感受性物質を層状態で前記殻壁に含有、付着又は被覆させた。
【００１４】請求項４に係る発明では、前記超音波感受性物質を塊状に分散した状態で前記殻壁に含有又は付着させた。
【００１５】請求項５に係る発明では、前記殻壁の厚さ

を０．００１～５０μｍの範囲に規定した。

【００１６】請求項６に係る発明では、前記殻壁によって形成された中空部に薬物を坦持させた。

【００１７】請求項７に係る発明では、前記薬物をガスと併存させた状態で前記中空部に坦持させた。

【００１８】請求項８に係る発明では、超音波感受性物質として、ポルフィリン誘導体又はキサンテン誘導体を採用した。

【００１９】請求項９に係る発明では、薬物坦持体に０．１～１０００ワット／平方センチの出力の超音波を照射することにより前記薬物担持体を破壊することとした。

【００２０】

【発明の実施の形態】本発明は、治療用薬物を坦持して目的部位まで搬送しうる薬物坦持体に超音波感受性物質を含ませることにより、薬物を坦持した前記薬物坦持体が目的部位において超音波を照射されたときに、前記超音波感受性物質に化学変化又は物理変化を生じさせて前記薬物坦持体を破壊して、薬物を放出させることにその第１の特徴を有している。

【００２１】本発明は、単に超音波による振動作用のみでカプセル殻を破壊して内部の薬物を放出させる方法に比して、該カプセルの破壊が超音波の照射条件にさほど影響されないので、０．１～１０００ワット／平方センチという比較的広い範囲の超音波エネルギーを採用することが可能である。

【００２２】したがって、従来のように、非常に困難な超音波照射の条件設定を行うことなく、体内の目的部位において、薬物坦持体の共鳴周波数以外の超音波でも効果的に該薬物坦持体を破壊して薬物を放出することができる。

【００２３】また、本発明は、薬物坦持体に所定の厚さを有する殻壁によって中空部を形成し、該殻壁に超音波感受性物質を含有、付着又は被覆させることに第２の特徴を有している。すなわち、薬物担持体は、圧力等の機械的エネルギーには充分耐えられる一方、前記超音波感受性物質の化学変化又は物理変化によって容易に壊れる構造にデザインされている。

【００２４】具体的には、薬物担持体の形状はカプセル状等とされ、超音波感受性物質が層状態又は塊状でカプセルを構成する殻壁に含有、付着又は被覆される。前記超音波感受性物質が層状態となっている場合は、該超音波感受性物質の変質の影響を前記殻壁全体に及ぼすことが可能となり、一方、前記超音波感受性物質が塊状の場合は、該超音波感受性物質を前記殻壁に局所的に存在させることにより、確実に該殻壁を破壊することが可能となる。なお、薬物担持体自身の構成材料として、超音波感受性物質を後述する基質材料に均一に混合したものを用いてもよい。この場合は、殻壁の破壊が均等に行われると共に、薬物担持体の製造が容易になる。

【００２５】さらに、本発明は、前記殻壁によって形成された中空部に薬物を坦持させるものであるが、前記薬物と共に所定量のガスを前記中空部に存在させてもよいことに第３の特徴を有している。後述するように、前記ガスの種類及び量は任意であるが、前記中空部の体積の０．０１～５０％の範囲で設定されるのが好ましい。まず、本発明に係る薬物坦持体の成分及び構造について説明する。

【００２６】ここで、「薬物坦持体」とは、治療用薬物を坦持して体内又は体表面の目的部位まで搬送しうるキャリアーであり、その形状は特に限定されないが、製造の容易性、製造コスト等からみて、殻壁によって外界と隔別された中空部を有するカプセル形状が好ましい。

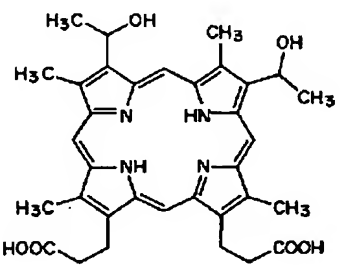
【００２７】薬物坦持体の大きさは通常０．０１～１００μｍの範囲で適宜設定される。０．０１μｍ未満では体外に排泄されて効果が不十分になり、１００μｍより大きいと血管内に血流障害を起こす危険性がある。

【００２８】前記薬物坦持体を構成する基質材料としては、各種の生体適合ポリマー、アルブミン、リポゾーム、糖等の物質を用いることができる。

【００２９】また、プロドラッグ化修飾を施された薬物坦持体を使用することにより、標的組織部位への選択的移行性の改善、水溶性の増加、吸収の促進または副作用の軽減等を図ることもできる。この場合は、体内において前記修飾の目的を達成した後に酵素的または非酵素的に元の薬物坦持体に復元され、超音波に対する感受性等を回復することが可能となる。プロドラッグ化修飾を施された薬物坦持体は本発明の範疇に含まれる。なお、薬物坦持体に坦持される薬物にプロドラッグ化処理を施したものを適宜用いても良い。

【００３０】「超音波感受性物質」とは、所定の周波数、強度を備えた超音波により、後述するように様々な機構を経て活性化されたり、自己又は他の物質に化学変化を生じさせたり、或いは自己の構造を変化させたりする等の何らかの変化を生じる物質のことである。前記超音波感受性物質としては、フロレシーン（fluorescein）、メロシアニン等が挙げられるが、毒性の面と生体に対する親和性の点でポルフィリン誘導体またはキサンテン誘導体が好ましい。前記ポルフィリン誘導体またはキサンテン誘導体として、具体的には、以下に示される構造式を有するヘマトポルフィリン、

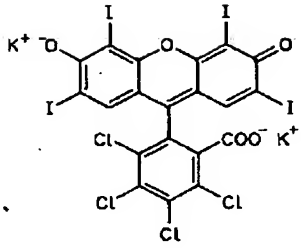
【化１】



5

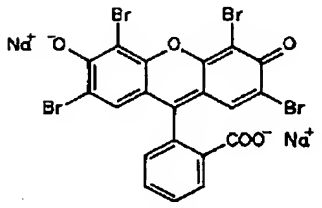
ローズベンガル、

【化２】



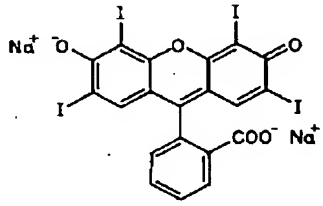
エオジンＹ、

【化３】



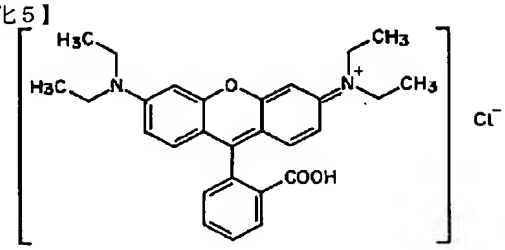
エリスロシン、

【化４】



ローダミンＢ、

【化５】



が挙げられる。

【００３１】そして、薬物坦持体の構造としては、図１に記載されるように、不定形の薬物坦持体１中に薬物２と超音波感受性物質３の塊が適当な間隔で分散しているものであってもよいが、薬物坦持体自体に所定の厚さを有する殻壁によって中空部を形成し、該殻壁に上記超音波感受性物質を含有、付着又は被覆させることが該薬物担持体の効果的な破壊を可能とする点で好ましい。

【００３２】前記中空部は、薬物坦持体の内部に形成されるのであれば、その個数は特に限定されず、一つであっても複数であってもよい。また、その形成箇所も特に限定されるものではないが、薬物の放出を良好に行うために、薬物坦持体の表層部に形成されることが好ましい。なお、薬物坦持体の形状自体を、前記所定の厚さを有する殻壁の層によって構成されたカプセル状とすることも本発明の範囲に含まれる。

6

【００３３】ここで、前記殻壁の厚さは、通常、０．００１～５０μｍの範囲内で決定される。殻壁の厚さが０．００１μｍ未満となると、衝撃により殻壁が破壊され易くなり、体内の目的部位に到達する前に前記殻壁が破壊されて内部の薬物が流出してしまうおそれがある。一方、５０μｍ以上になると、超音波感受性物質の作用によっても前記殻壁を破壊することが困難となり、また、たとえ一部の殻壁が破壊されても、破壊不能な殻壁部分が残存してしまい、薬物の放出を妨げるおそれがある。

【００３４】薬物坦持体に対して超音波感受性物質を含有させるに際しては、該薬物坦持体が殻壁構造を備えている場合は、該殻壁中に前記超音波感受性物質を含有、付着又は被覆させることが好ましい。

【００３５】具体的には、超音波感受性物質３の層を図２（ａ）に示すように殻壁１ａの外表面に被覆しても、図２（ｂ）のように殻壁１ａの内周面にコーティングしてもよく、また、図２（ｃ）のように殻壁１ａの内部に層状態で存在させてもよい。なお、超音波感受性物質３の層は図２に示すような連続的な層構造でなくともよく、また、殻壁１ａと同心円状に存在させなくともよい。

【００３６】また、超音波感受性物質３を塊状に分散させた状態で殻壁１ａに含有又は付着させてもよい。すなわち、図３（ａ）及び図３（ｂ）に示すように、超音波感受性物質３の塊を前記殻壁１ａの外表面及び内表面に付着させてもよく、図３（ｃ）のように前記殻壁１ａの内部に適当に分散されてもよい。この場合は各塊は殻壁１ａから一部突出していてもよく、また、突出していなくてもよい。

【００３７】そして、図３（ｄ）に示すように、超音波感受性物質３の塊が殻壁１ａを貫通して外界及び内部空間にその一部がそれぞれ露出するような構造としてもよい。図３に示した場合にあっては、前記超音波感受性物質３の塊は前記殻壁１ａに均一に分散していてもよく、粗密に分散していてもよい。また、各塊の形状は特に限定されるものではなく、球形以外の様々な形状であってもよい。

【００３８】なお、図２及び図３において、４は殻壁１ａによって形成された中空部であり、該中空部に所定種類の薬物が坦持される。

【００３９】次に、上述した薬物坦持体の使用方法について図４を参照しつつ説明する。

【００４０】所定種類の薬物を坦持した上記薬物坦持体は注射器等の薬物投与具を使用して、又は経口投与や経皮投与、或いは特殊な方法ではイオン化した薬物坦持体を用いたイオントフォーレシス手法等によって体内に注入される。

【００４１】そして、カテーテルや内視鏡の使用が可能

である場合は、治療用超音波発生素子をカテーテルまたは内視鏡の先端に取り付け、患者の体内に導入して患部に到達させる。

【００４２】図４（ａ）及び図４（ｂ）はそれぞれ本発明の実施において使用される超音波発生素子の取り付け態様を示す断面図であり、図４（ａ）は、超音波発生素子を内視鏡の先端部に取り付けた場合の構造を、また、図４（ｂ）はカテーテルの先端部に取り付けた場合の構造を示す。

【００４３】図４（ａ）に示す態様においては、内視鏡を構成する細管５の内部に、図示しない光ファイバー及び後述する超音波振動素子を作動させるための配線を含む微少中心管６を延設し、細管５の先端に、軸線方向に中空部を有する円筒形状の第１の超音波振動素子９及び第２の超音波振動素子１０を同心円状に配設している。超音波振動素子としては、たとえば圧電素子の両面に電極を取り付けたものが挙げられ、この場合は該電極間に超音波周波数の電気信号を印加することにより、超音波が放射される。８は外部の映像を図示しない光ファイバーに伝達するためのコア部であり、前記中空部に埋め込まれている。また、細管５と微少中心管６との間隙は薬物供給路７とされており、細管５の先端側の周面に適当な間隔で開口する貫通孔１１に連結されている。

【００４４】そして、前記第１の超音波振動素子９と第２の超音波振動素子１０はそれぞれの周波数特性が異なっており、両者の作動を制御することにより２種類の周波数が混合されて内視鏡の軸方向とは垂直の方向（矢印方向）に発振されるようになっている。このように複数種類の超音波を組み合わせて放射するのは、複雑な超音波波形の方が薬物坦持体の破壊効率が向上するからである。なお、上記構造を有する第１及び第２の超音波振動素子をカテーテルの先端に取り付けてもよい。一方、図４（ｂ）に示す態様においては、周波数特性の異なる第１の超音波発振素子９及び第２の超音波発振素子１０は共に中実の円筒形状とされて、カテーテルの軸線方向に積層されている。

【００４５】したがって、両者の作動を制御することにより、カテーテルの軸線方向（矢印方向）に２種類の周波数を有する超音波が発振されるようになっている。

【００４６】なお、上記構造を有する第１及び第２の超音波振動素子を内視鏡の先端に取り付けてもよい。

【００４７】さて、内視鏡またはカテーテルの先端が患部組織に到達したことを確認後、開口部１１を介して薬物供給路７から薬物坦持体を患部に向けて放出する。それと同時にまたは所定時間経過後に、超第１及び第２の超音波振動素子を作動させると周波数の異なる超音波が患部に放射されて、患部組織中に存在する薬物坦持体を破壊する。したがって、薬物坦持体内の薬物は患部組織部位周辺だけに限定して投与される。

【００４８】前記内視鏡またはカテーテルに対する患部の相対位置を考慮して、好適な超音波の照射が得られるように機器を選択することが好ましい。また、前記内視鏡またはカテーテルの直径は１ｍｍから５ｃｍ程度の範囲のものを適宜選択して使用できる。

【００４９】なお、上記超音波発振素子を３種以上取り付けてもよい。その場合は、更に複雑な超音波波形を生成することができるので、薬物坦持体の破壊効率が更に向上する。薬物坦持体が破壊されやすい形状である場合等は一の超音波振動素子を用いてもよい。

【００５０】一方、カテーテルや内視鏡が使用できない場合は、図５に示すように、例えば、柔軟な合成樹脂等からなる基体１２の凹部に上記したのと同様の特性を有する第１の超音波振動素子９及び第２の超音波振動素子１０を積層して配置した治療用超音波発生装置を、患部に対応する皮膚上に好ましくは複数個載置して超音波を患部（矢印方向）に向けて照射する。図示するように、基体１２には超音波振動素子の積層物を複数設けることが好ましい。基体１２は患者の体の形状に合わせて湾曲可能であるので超音波を患部に集中させることが可能である。前記第１及び第２の超音波振動素子の直径は通常５ｃｍ～１０ｃｍの範囲で適宜設定される。なお、前記第１の超音波振動素子９及び第２の超音波振動素子１０はフッ素化合物のような柔軟性のある発振材料で構成される方が、装置全体の柔軟性を維持し、皮膚などへの密着性を確保するためにより好ましい。

【００５１】そして、患部に集中した超音波エネルギーはそこに存在する薬物坦持体を破壊して、患部に内部の薬物を放出する。

【００５２】このように、本発明においては、薬物坦持体に超音波感受性物質を含ませることにより、超音波のみでは破壊が困難であった薬物坦持体を容易に破壊して所望の体内部位において薬物の放出をコントロールすることが可能となる。

【００５３】なお、薬物坦持体の基質材料に癌細胞、血栓、臓器、動脈硬化した血管等の患部組織に選択的に結合する抗体等の物質を含ませた場合は、薬物坦持体を患部組織に集積させることができるので、該患部組織に集積した薬物坦持体を超音波を用いて破壊して薬物を局部的に高濃度に投与することが可能となる。

【００５４】次に、本発明において使用される超音波の条件について説明する。

【００５５】本発明に係る薬物坦持体の破壊のために照射される超音波の出力は０．１～１０００ワット／平方センチの範囲で適宜設定される。超音波の出力が０．１Ｗ／ｃｍ２以下だと、超音波感受性物質を活性化させるだけのエネルギーが不足し、１０００Ｗ／ｃｍ２以上になると、熱発生が多すぎるために、生体にダメージを与えてしまう。

【００５６】また、超音波の周波数は１０ｋＨｚ～１００ＭＨｚの範囲で適宜設定されるが、特に、２０ｋＨｚ

～１０ＭＨｚの範囲が好ましい。この周波数帯の超音波によれば比較的低いエネルギーで後述するキャビテーションを発生させて薬物坦持体を効率的に破壊することが可能となる。

【００５７】そして、上述したように、複数の周波数を組み合わせることでより効率よく超音波感受性物質を活性化させて薬物坦持体を破壊することも可能である。例えば、一定の周波数の超音波を照射中に、断続的にこれとは異なる周波数に切り替えることで、後述するキャビテーションの発生を意識的に増強させたり、抑制して薬物坦持体を破壊又は分解できる。

【００５８】実例を挙げると、１００ｋＨｚで患部に超音波を連続照射している間に、２７０ｋＨｚの周波数に短時間（０．００１ｓｅｃ－１０ｓｅｃ）パルス状に切り替えることにより一層の破壊効果が得られた。超音波の周波数を一定範囲内で連続可変させても同様の効果が期待される。この現象は薬物坦持体の共鳴運動を一時的に停止させることにより破壊力が増大したものと考えられる。

【００５９】ここで、薬物坦持体の破壊の機構について説明する。

【００６０】一般に、液体中である値以上の超音波エネルギーが与えられると、キャビテーションと呼ばれる微小な空泡が発生する。キャビテーションの発生メカニズムに関しては、例えば、Robert E.Apfel:"Sonic effervescence:tutorial on acoustic cavitation",Journal of Acoustic Society of America 101(3):1227-1237,March 1997,Atchley A ,Crum L:"Ultrasound-Its chemical,Physical and biological effects:Acoustic cavitation and bubble dynamics",Ed Suslick K,ppl-64,1988 VCH Publishers,New Yorkに記載されているが、以下に簡単に説明する。キャビテーションとは、ある音響学的振動下で、水溶液に溶けているガスが気泡となるか、或いは、既に存在していた極微少な泡が、振動、又は拡大、縮小を繰り返して気泡となることである。

【００６１】そして、このキャビテーションはその大きさを維持できない程度の大きさになると崩壊するが、この崩壊は急激に起こるので、そのときに様々なエネルギーが局所的に発生することが知られている。

【００６２】すなわち、上記キャビテーションの崩壊の際には、その中心部に６０００～７０００度のホットスポットが形成され、振動等の機械的エネルギーの他に可視光線、紫外線等の電磁波、熱、プラズマ、電磁場、衝撃波、フリーラジカル、熱等の様々なエネルギーが局所的に発生すると考えられている。

【００６３】本発明における超音波感受性物質は、キャビテーション崩壊の際に生じる上記した様々なエネルギーによって活性化されたり、化学変化を生じさせたり、構造を変化させたりするものと考えられる。

【００６４】例えば、本発明における超音波感受性物質の一つであるローズベンガルは５３０ｎｍの波長の光又は紫外線で励起され、活性化される。したがって、ローズベンガルの活性化はキャビテーション崩壊の際に発生する紫外線によって引き起こされているものと考えられる。

【００６５】ところで、超音波感受性物質が存在する液体中ではキャビテーション発生のための超音波エネルギーの閾値が低くなることが知られている。したがって、薬物坦持体内に含有された超音波感受性物質は、薬物坦持体近傍でのキャビテーション発生を選択的に誘起し、かつ、キャビテーションの崩壊により生じたエネルギーによって自分自身を活性化等させて薬物坦持体を破壊するという効果を奏する。

【００６６】一方、液体中に微小な泡が存在していることによっても、キャビテーション発生のための超音波エネルギーの閾値が低くなることが知られている。

【００６７】したがって、薬物担持体内に所定量のガスを存在させることによって、超音波照射時にキャビテーションを効果的に発生させ、該キャビテーション崩壊の際に生じるエネルギーを薬物担持体の破壊に有効に利用することができる。前記ガスの種類及び量は任意であるが、その量は、薬物坦持体内の中空部の体積の０．０１～５０％の範囲で設定されることが好ましい。前記ガスの量が前記中空部体積の０．０１％未満であると、キャビテーションの発生を効果的に誘因させることができず、また、前記ガスの量が前記中空部体積の５０％を越えると、目的部位に到達するまで薬物坦持体の強度が保たれず、また、搬送される薬の量が制限される。

【００６８】なお、キャビテーションの崩壊の際に生じる可視光線、紫外線等の電磁波、熱、プラズマ、電磁場、衝撃波、フリーラジカル、熱等の様々なエネルギーを用いて直接、患部組織の治療に用いることも可能である。

【００６９】例えば、患部組織の近傍で超音波を発生させることにより、通常は皮膚に吸収されて体内には届かない紫外線を、超音波に由来するキャビテーションの崩壊によって体内の患部組織の近傍で発生させ、その殺菌作用により患部を治療することが可能となる。

【００７０】つまり、体内で超音波によってキャビテーションを発生させ、この崩壊時に生じるエネルギーにより患部の治療を行う方法を実施することができる。

【００７１】この方法によれば、体内のあらゆる箇所において自在に紫外線等のエネルギーを発生させ、これによって患部の治療を行うので、薬物治療に固有の副作用による影響を考慮する必要がない。

【００７２】本発明は、以下に述べるような形態で実施することが可能である。

【００７３】〔癌治療〕抗癌剤であるシスプラチンをポリマーのカプセルで包み、超音波感受性物質を該カプセルの外表面にコーティングしたものを静脈注射する。シ

スプラチンはポリマーで覆われているため、前記カプセルは静脈注射されても毒性（副作用）がなく、血液中を流れているだけである。

【００７４】しかし、前記カプセルが癌組織中の血管内を流れているときに超音波を照射すると、前記カプセル表面の超音波感受性物質が活性化され、シスプラチンを包んでいるカプセルを分解して、該組織中でシスプラチンが高濃度で放出される。

【００７５】したがって、癌が位置している限定された部位での高濃度の抗癌剤の投与が可能となる一方、正常細胞組織はシスプラチンの強い毒性から免れることが可能となる。

【００７６】この方法は、血管が多く存在する肝臓癌、脳腫瘍等の疾病に特に効果が得られる。超音波の照射方法としては、皮膚の表面から腫瘍部分に照射するか、開腹手術中に直接超音波を癌組織に照射することもできる。

【００７７】また、内視鏡に超音波素子を取り付け、体の内部から超音波を照射することも可能であり、その場合は、胃の内部や大腸の内側腔から大腸癌等に直接超音波を照射することもできる。

【００７８】上記カプセルの投与経路は、静脈注射の他、経口投与による腸管からの吸収、リンパ管を経由して直接患部への注入及び経皮投与等の様々なルートからケースに合わせて適当な経路が選択される。

【００７９】ところで、上記超音波感受性物質としてフォトフィリンを使用した場合には、フォトフィリン自体に癌細胞に対する親和性があるので、シスプラチン入りの上記カプセルは癌組織に集中して高濃度に蓄積される。

【００８０】そして、この状態で超音波を照射することにより、癌組織中に更に高濃度にシスプラチンを投与することが可能となる。

【００８１】なお、フォトフィリンは超音波によって活性化されると、殺細胞作用を生じる性質をも有するので、この場合は、シスプラチンと併せて相乗的に抗癌作用が増強される。

【００８２】また、腹腔内に転移した癌や膀胱癌の場合には、抗癌剤を内包するカプセルを直接腹腔内に注射してその後、超音波を皮膚表面から腹腔全体に向けて照射する方法が考えられる。膀胱癌の場合は尿道から前記カプセルを膀胱内に充満させ、下腹部の皮膚表面から超音波を照射することで膀胱癌を治療することができる。これらの場合は、治療用の超音波を照射している間に、診断用の超音波で薬物の放出状態を観察できるという利点を有する。

【００８３】〔血栓溶解治療〕血栓溶解剤は心筋梗塞や脳梗塞の治療薬として使われている。しかし、血栓をできるだけ早く溶解させるために多量に投与すると逆に血液が凝固しにくくなり、多出血を起こす危険がある。

【００８４】そこで、ウロキナーゼ等の血栓溶解剤を超音波感受性物質を含む生体適合ポリマー又はアルブミン製のカプセルで包み、これを血管内に注射する。このカプセルは通常の状態では破壊されないので血管内で溶解作用を引き起こすことがない。

【００８５】そして、例えば心筋梗塞の場合、冠動脈の末梢血管等の血栓が存在する部位に前記カプセルが到達すると、上記したような装置を用いて超音波を体外又は体内から照射することにより前記カプセルを破壊して血栓溶解剤を局所的に高濃度で放出する。

【００８６】具体的には、図６に示すように、血栓の近くまで図４の超音波発振子付カテーテルまたは内視鏡を血管内に挿入し、血栓溶解剤入りカプセルを血栓の直ぐ上流から放出し、同時に超音波を発振させる。前記カプセルは超音波により活性化された超音波感受性物質の作用により破壊されて、内部の血栓溶解剤が血栓部位に放出される。

【００８７】なお、超音波で破壊されなかったカプセルは再度患部に流れ着く際に破壊されて利用される。そして、再度患部に到達するまでの間は前記カプセルが破壊されることはないので、出血の要因になることはない。

【００８８】また、カプセルの外表面に血栓に特異的に親和性がある物質或いは抗体を予め付与した場合は、血栓に該カプセルが高濃度に集積する。その状態で血栓部位に超音波を照射すると該カプセルが破壊されて血栓の近傍で効果的に血栓溶解剤を投与することが可能となる。血栓に親和性がある物質はLanzaらによって報告（Circulation, 1995, 92.Suppl I:1-260)されている。

【００８９】このようにすることで、出血等の副作用を起こさずに効率的に血栓溶解治療が可能となる。

【００９０】〔血管治療〕動脈硬化等が原因となって血管狭窄が起こった場合、近年はバルーンカテーテルで血管内腔を押し広げて血液の流れを再開させる手術治療が盛んに行われている。

【００９１】また、上記手術後、再度、血管狭窄が起きないように、金属製のステントで血管内腔を広げた状態で固定するような治療も盛んに行われている。

【００９２】しかし、いずれのケースでも、血管の内壁にはある程度の損傷が与えられる。損傷を受けた血管組織は血管を元の状態に回復すべく、血管組織の増殖を伴う修復を行うが、この修復過程で過度の修復が起こり、血管の再狭窄を起こすケースが５０％以上に上り、この治療の欠点とされている。

【００９３】そこで、図７に示すように、バルーンの材質として、フォトフィリンを内部に坦持した薬物坦持体を混入させたものを採用し、中心部に超音波発生素子を位置させたバルーンカテーテルを血管内に挿入し、目的部位においてバルーンを膨張させて、血管壁に密着させる。

【００９４】この状態で前記カテーテルの軸線とは垂直

方向に超音波を発生させると、前記バルーンの血管壁に接する部分に位置する薬物坦持体が破壊されて、内部のフォトフィリンが血管壁内に直接注入されるる。

【００９５】フォトフィリンは超音波で活性化されると血管組織の修復過程をある程度阻害する性質を有するので、バルーンによって損傷を受けた血管壁の過度の修復を抑制することが可能となり、再狭窄を予防できる。

【００９６】この実施の形態においては、フォトフィリンは患部治療用の薬物として薬物坦持体内に坦持されており、薬物坦持体に含まれる該坦持体破壊用の超音波感受性物質は任意とされているが、該超音波感受性物質としてフォトフィリンを用いてもよい。

【００９７】なお、血管治療で使用できる患部治療用の薬物としては、血管内壁へ投与される遺伝子、ヘパリン、放射性物質等が挙げられる。

【００９８】〔止血剤としての使用〕肝癌に対し、現在、癌組織の栄養血管内にエタノールを注入し、該血管の内壁に損傷を与え、人工的に血栓を作って該血管を閉鎖するとか、特定種類の液体を注入して血管を詰まらせる等の方法で癌細胞の増殖を防止する治療法が行われている。

【００９９】その代わりに、超音波により活性化されることにより血管内壁損傷剤としての作用を発揮するローズベンガル入り薬物坦持体と、これとは別に、血液凝固剤としての作用を有するトロンビン入り薬物坦持体とを同時に血管内に注入し、患部において超音波を照射する方法を採用する。

【０１００】この実施の形態では、ローズベンガルは患部治療用の薬物として薬物坦持体内に坦持されている。そして、両薬物坦持体に含まれる該坦持体破壊用の超音波感受性物質は任意であるが、ローズベンガルを用いてもよい。

【０１０１】この方法においては、前記薬物坦持体が超音波によって破壊されて、その内部のローズベンガルが患部において放出されるが、その際、ローズベンガル自身が超音波によって活性化されて血管壁に損傷を与え、血栓が形成される。

【０１０２】そして、これと同時に、別個の薬物坦持体から放出されたトロンビンが血液を凝固させる。したがって、患部における血流が停止される。

【０１０３】このように２種の薬物坦持体を組み合わせることにより止血剤としての相乗効果を得ることができる。

【０１０４】上記した方法は肝癌の治療の他に、今までほとんど手がつけられなかった交通事故等による臓器出血の止血に適している。

【０１０５】〔薬物の経皮吸収〕超音波を併用した薬物の経皮投与については既に知られているところである。例えば、特願平９－１６６３３４号の明細書に記載されるように、多数の微細な透孔を有し、内部に液体が含まれた円板状の板体からなる処理装置が開発されている。この装置においては、キャビテーション発生現象を使用して皮膚の表面に微細な穴を開けることにより、痛みを伴うことなく効率的に、薬物の投与或いは体液の採取を行うことが可能である。

【０１０６】この実施の形態では、上記処理装置中の前記透孔に超音波感受性物質を含んだ薬物坦持体を配置させる。

【０１０７】以下、図８を参照して説明する。

【０１０８】本実施例においては薬物の経皮投与装置１３を、たとえば、１μｍ～１ｃｍの範囲の比較的薄い合成樹脂材料等からなるフィルムから構成し、その内部に、円形空間１４を形成する。

【０１０９】経皮投与装置１３の底側フィルム１５には、円形空間１４から外部に連通する複数の透孔１６が形成されている。透孔１６の直径は、たとえば、０．１μｍ～３ｍｍの範囲とすることができる。なお、図８の例では透孔１６は均一に分布しているが、必要に応じて粗密に設けてもよい。また、透孔１６の断面形状は円に限らず、星形、多角形等の不整形でもよい。透孔１６の密度は１平方センチ当たり１個から１００万個の範囲とすることができる。

【０１１０】一方、経皮投与装置１３の上側フィルム１７には超音波振動素子１８を取り付ける。この超音波振動素子１８は、経皮投与装置１３と一体的に形成してもよいが、これとは別に独立した部材として、経皮投与装置１３の上側フィルム１７に押しつけるようにしてもよい。

【０１１１】薬物の経皮投与装置１３を使用するに際しては、透孔１６内に薬物坦持体１９を配置させ、円形空間１４及び薬物坦持体１９内部の坦持空間２０を液体薬物２１で満たす。

【０１１２】そして、経皮投与装置１３の底側フィルム１５を皮膚の表面に圧着し、超音波振動素子１８に駆動信号を供給して超音波を発生させる。すると、薬物坦持体１９が破壊されて透孔１６が開通すると共に、円形空間１４内の液体薬物２１中にキャビテーションが発生し、このキャビテーションの崩壊時に生じる高速の液流が透孔１６を通過して皮膚に達し、その表面に微細な穴が形成される。液体薬物２１はこの穴を通して体内に吸収される。

【０１１３】このようにすることで、透孔１６が比較的大きい場合でも経皮投与装置１３の保管時に透孔１６から液体薬物が流出することがない。一方、薬物坦持体１９は超音波によって破壊されるので使用の際は確実に透孔１６を開通させることができる。

【０１１４】また、薬物坦持体１９中の超音波感受性物質はキャビテーション発生の閾値を低下させるので、低い超音波エネルギーで液体薬物２１中にキャビテーションを発生させることができる。これにより、皮膚に照射

される超音波エネルギーを少なくすることが可能となり、皮膚に悪影響を与えるおそれが少なくなる。

【０１１５】この装置を用いて皮膚内に投与する薬剤としては、抗アレルギー剤、インシュリン、各種ホルモン、抗癌剤、抗炎症剤、麻酔薬、抗凝固因子（ヘパリン、ウロキナーゼ）、抗生物質、各種ビタミン、ステロイド、昇圧剤、降圧剤、向精神剤、発毛又は脱毛剤等がある。

【０１１６】〔感染症治療〕ＵＶ光による殺菌消毒効果は良く知られているが、ＵＶ光は液体中での通過性がきわめて悪く、直ちに減衰するために、もっぱら大気中において医療器具等の表面の消毒に用いられているのみである。

【０１１７】ところで、超音波感受性物質であるローズベンガルは、超音波によるキャビテーション発生の閾値を低下させる作用をも有することが知られている。

【０１１８】そこで、この性質を利用して、体内外における感染症の治療に体内における感染症の治療に超音波を用いることができる。

【０１１９】すなわち、体内における感染症治療においては、ローズベンガルを含む坦持体を注射等により患部の深部まで侵入させ、その状態で患部に向けて超音波を照射すると、該坦持体周辺に比較的低い超音波エネルギーでキャビテーションが発生し、既述したように、その崩壊時にＵＶ光が発生する。

【０１２０】したがって、体内の患部に至近距離からＵＶ光を照射して、殺菌することが可能となるので、感染症の治療に応用することが可能となる。

【０１２１】また、この方法は、各種抗生剤を使用する必要がないために、耐性菌を作らない等の利点がある。

【０１２２】次に、皮膚感染症の場合は、皮膚吸収促進剤を坦持した薬物坦持体であって、ローズベンガルをその表面に被覆したものを皮膚表面に塗布する。ローズベンガルは皮膚に比較的浸透し易いので、前記薬物坦持体は皮膚表面部分に若干浸透する。　この状態で超音波を皮膚に向けて照射すると、前記皮膚吸収促進剤が皮膚内に放出され、皮膚のバリアー機能が低下または消失するため、通常、皮膚に吸収されにくいインシュリンのような薬物が皮膚内に吸収される。

【０１２３】なお、上記方法は皮膚感染症の治療以外にも、水虫、ウイルス性の水疱、乾癬、疥癬、皮膚癌、ＡＩＤＳによるカポジ肉腫の治療等への応用が可能である。

【０１２４】〔糖尿病治療〕インシュリンを内包する薬物坦持体を血管内に注入し、必要な時に超音波を体内に向けて照射することにより、前記薬物坦持体を破壊して内部のインシュリンを体内に放出することにより、糖尿病の治療を行うことができる。この場合は、超音波を照射する時間及び強度等を調整することにより、簡単な操作で定期的にインシュリンを投与することが可能となる。

【０１２５】また、血液中の赤血球を上記薬物坦持体として使用することも可能である。例えば、血液中から赤血球を分離し、各赤血球内にインシュリンを注入した上で超音波感受性物質であるフォトフィリンを赤血球の膜の表面に付着処理する。

【０１２６】この処理済みの赤血球を患者の体内に輸血等して供給すれば、赤血球は約１００日間の寿命があるので超音波を照射しない限りその期間中に破壊されることはないが、必要に応じて体外から超音波照射してインシュリンを放出することができる。

【０１２７】この場合は、人体に適合し易い材質である赤血球から薬物坦持体を構成するため、人体からの拒絶反応を抑制することが可能となる。

【０１２８】

【実施例】本発明の効果を確認するために行った実験例について説明する。ただし、本発明をこれに限定するものでは決してない。

【０１２９】〔実験例〕アルブミンで包まれた微小中空球体を、ビーカー中に、５％ヒト血清アルブミンの１ｍｌ中に約１億個の割合で含有させ、超音波感受性物質であるローズベンガルによる処理を行ったものと、該処理を施していないものに分けた。

【０１３０】それぞれの微小中空球体を含んだビーカーに超音波を１ＭＨｚ、０．５Ｗ／ｃｍ２で３０秒照射し、照射後の微小中空球体の個数を数えた。

【０１３１】ローズベンガルでコーティングした微小中空球体はほとんど壊れていたが、未処理のものはまだ７０％の個数の形状が保たれていた。

【０１３２】このように、ローズベンガルの存在により、超音波の機械的エネルギーのみでは得られなかった破壊効果を得ることができた。

【０１３３】なお、ローズベンガルに代えてエオジン等の色素を用いても同様の結果を得ることができた。

【０１３４】

【発明の効果】請求項１、６、８又は９の発明では、薬物を坦持した前記薬物坦持体に体内の目的部位において超音波を照射することにより、薬物坦持体に含まれる超音波感受性物質を活性化させて該薬物坦持体を破壊して内部の薬物を効率的に放出させることができ、その際に、超音波照射条件を細かく設定する必要がない。

【０１３５】請求項２の発明では、薬物坦持体に所定の厚さを有する殻壁によって中空部を形成したので、該中空部の部分で薬物担持体を効果的に破壊することが可能となる。

【０１３６】請求項３の発明では、超音波感受性物質を層状態で前記殻壁に含有、付着又は被覆させたので、超音波感受性物質の変質の影響を殻壁全体に及ぼすことができる。

【０１３７】請求項４の発明では、超音波感受性物質を

局所的に存在させることにより確実に殻壁を破壊することが可能となる。

【０１３８】請求項５の発明では、前記殻壁の厚さを、０．００１～５０μｍの範囲内としたことにより、薬物の放出を確実なものとすることができる。

【０１３９】請求項７の発明では、前記薬物をガスと併存させた状態で前記中空部に坦持させたので、キャビテーションを効果的に発生させることが可能となる。

【図面の簡単な説明】

【図１】　薬物坦持体の実施の形態の一例を示すための断面構造図。

【図２】　薬物坦持体の実施の形態の他の一例を示すための断面構造図。

【図３】　薬物坦持体の実施の形態の更に他の一例を示すための断面構造図。

【図４】　本発明の実施において使用される超音波発生素子の取り付け態様を示す断面図。

【図５】　治療用超音波発生装置の一態様を示す断面図。

【図６】　本発明の薬物坦持体を血栓溶解治療に適用した場合を説明するための拡大断面図。

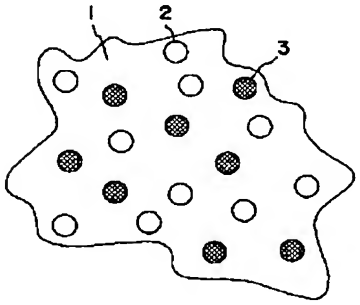
【図７】　本発明の薬物坦持体を血管治療に適用した場合を説明するための拡大断面図

【図８】　本発明の薬物坦持体を応用した経皮投与装置の断面図

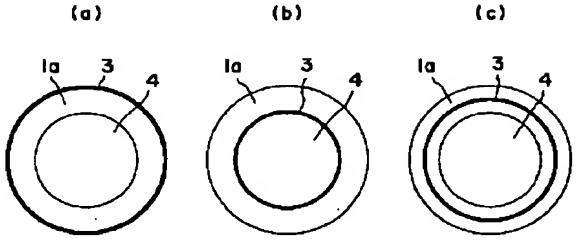
【符号の説明】

１	薬物坦持体
１ａ	殻壁
２	薬物
３	超音波感受性物質
４	中空部
５	細管
６	微少中心管
７	薬物供給管
８	コア部
９	第１の超音波振動素子
１０	第２の超音波振動素子
１１	開口部
１２	基体
１３	経皮投与装置
１４	円形空間
１５	底側フィルム
１６	透孔
１７	上側フィルム
１８	超音波振動素子
１９	薬物坦持体
２０	坦持空間
２１	液体薬物

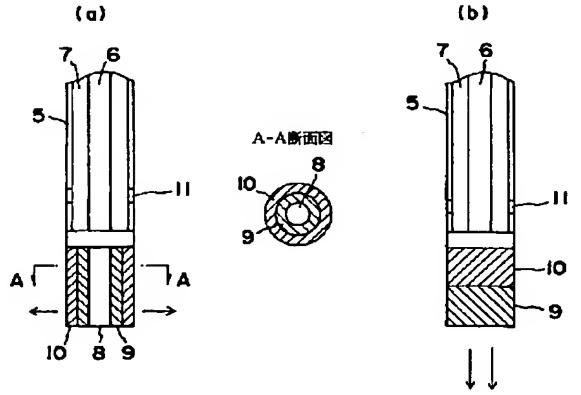
【図１】



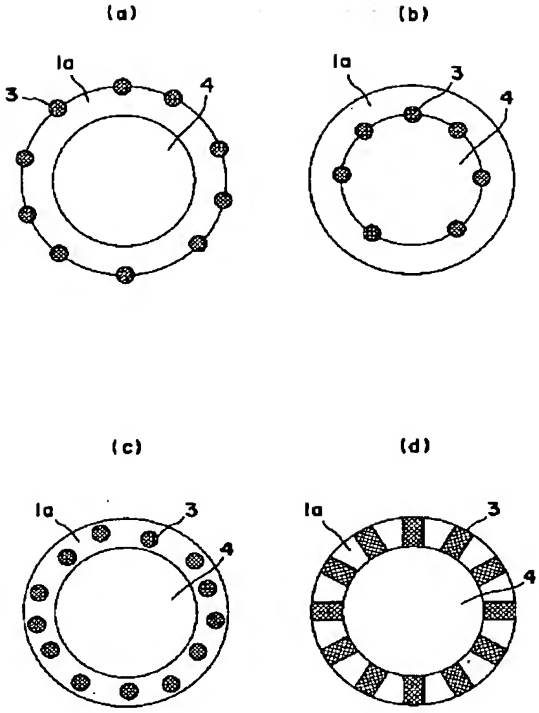
【図２】



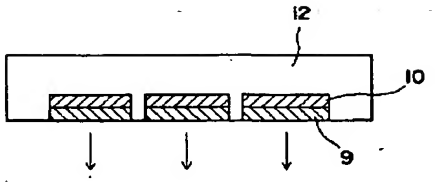
【図４】



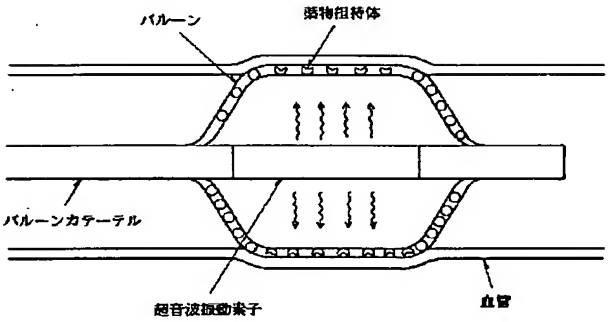
【図３】


(a)
(b)
(c)
(d)
1a
3
4

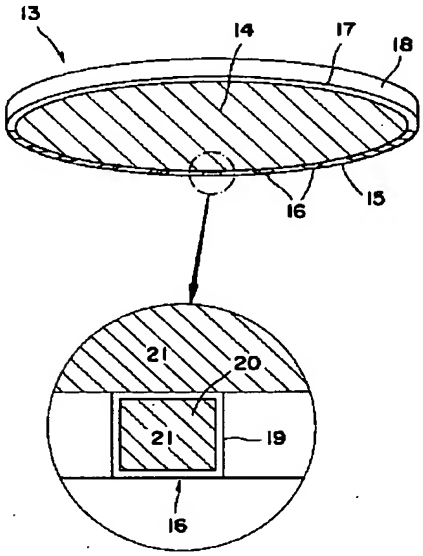
【図５】


12
10
9

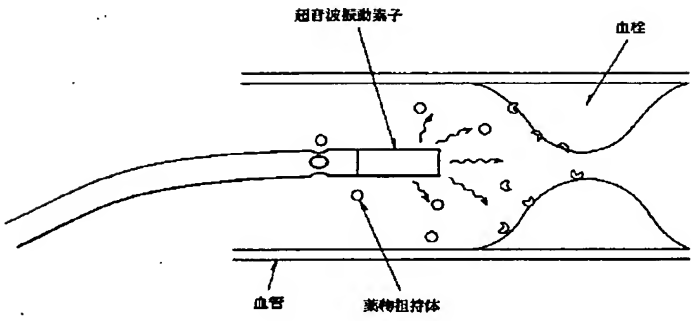
【図７】


バルーン
薬物担持体
バルーンカテーテル
超音波振動素子
血管

【図８】


13
14
17
18
16
15
21
20
21
19
16

【図６】


超音波振動素子
血栓
血管
薬物担持体